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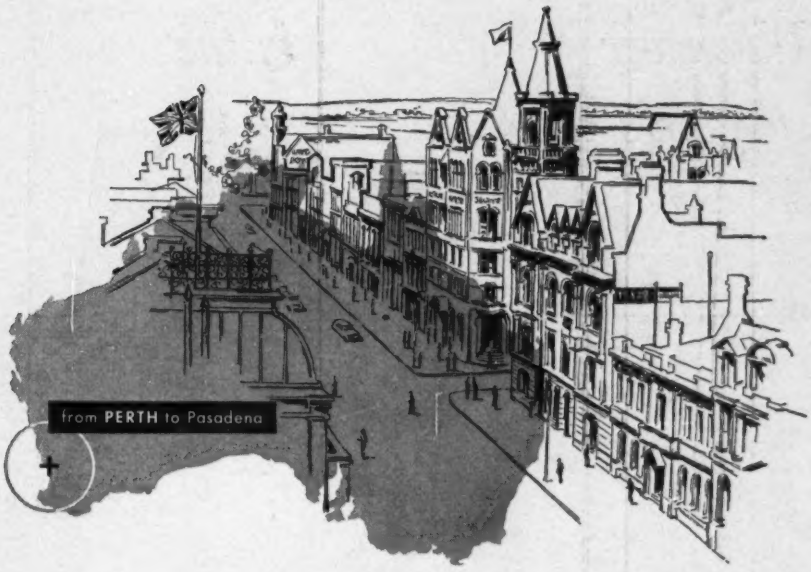

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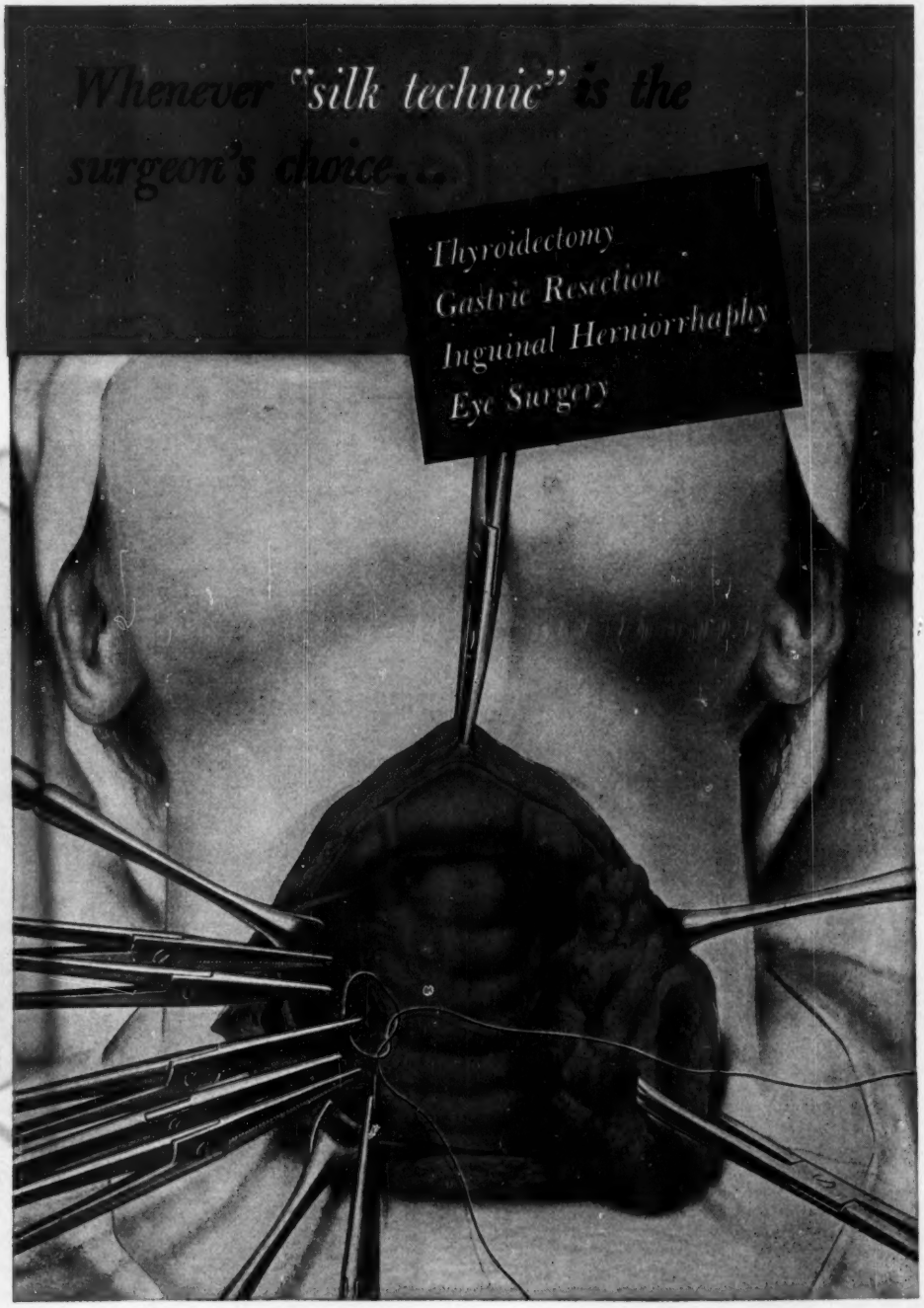
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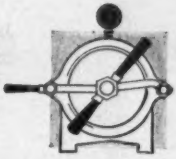

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Editorials

LOCAL RESECTION OF MALIGNANT TUMORS OF BONE

SARCOMAS of bone presenting no evidence of metastases are customarily treated by amputation if located in an extremity and by resection or excision if located in an accessible bone of other parts of the body. The prognosis following this type of management is relatively unfavorable and the five-year survival rate for bone sarcomas as a group is somewhat less than 20%. It is higher for extremity cases treated by amputation (excluding palliative amputation in patients with known metastases) than for the other group treated by resection or excision; however, the results in the writer's experience are not strikingly different for the two groups, especially if the resection is performed at an early stage.

Despite the fact that some worthwhile results have been obtained by massive resection of sarcomas of bones of the extremities, there is still reluctance on the part of surgeons to employ this method of treatment in any case in place of amputation. In view of important recent advances in both the principles and the practice of surgery and of increased knowledge of the pathology and roentgen diagnosis of bone tumors, it is appropriate to inquire if the time has not arrived when a considerable number of selected cases of sarcoma of extremity bones should be treated routinely be resection and repair of the defect by bone transplantation. Because of the much greater physical, mental, and social handicaps that result from amputation, many patients prefer treatment by resection unless the added risk of local recurrence is greatly increased. Also, resection may be justifiable when, for various reasons, the patient refuses amputation.

Resection and transplantation should be considered for any form of extremity bone sarcoma if the lesion is small and so situated that the main blood vessels and nerves of the limb can be preserved. Slow growth and short duration of the tumor are also favorable for resection.

Certain varieties of bone sarcoma are more favorable for resection than others although statistics on long-term survivals are scanty. Chondrosarcoma, reticulum-cell sarcoma, and giant-cell sarcoma may grow slowly and metastasize relatively late and consequently be more readily cured by local resection. Fibrosarcoma, angiosarcoma, and the round-cell tumor known as Ewing's sarcoma have a less favorable prognosis because of early metastases. On the whole, the osteogenic or bone-forming sarcomas, which comprise about 50% of all bone sarcomas, are less suitable for resection because of early invasion of local veins, the development of metastases, and the relatively high incidence of local recurrence. However, the recently described slowly growing and densely ossifying tumor, designated paraosteal osteoma, that begins outside of the shaft of a large bone, as the lower femur and the upper humerus, and later fuses with it, has sometimes proved to be a low-grade

osteosarcoma. In a small group of cases seen in our clinic, some apparently benign and others malignant, in which either wide local excision or resection was carried out, the majority have been controlled for periods ranging from one and one-half to six years after operation.

Resection should be done with the circulation interrupted by means of a tourniquet if it is possible to apply one. It should aim at removal of a segment of the bone that preferably extends 2.5 to 5 cm. beyond the limits of the tumor depending on the portion involved and the proximity to the neighboring joint. If the epiphysis is invaded and the joint is free, the entire end of the bone should be excised. If the tumor has extended to the surface of the joint, total arthrectomy including 1 or 2 cm. of the opposing bone should be carried out. With the segment should be included the overlying muscles that are in contact with, or are invaded by, the tumor. It may be possible to save muscles that are superficial to the bone or, less often, in contact with it on a side away from the tumor. After ligation of all bleeding points that have been clamped the constriction is released and hemostasis completed.

Autogenous tibial bone grafts are used to repair the skeletal defect whenever possible. If the defect is of the lower end or of a segment of the shaft of the femur which is not more than 10 cm. long, it can be repaired by two grafts taken from the tibia of the affected side, each graft comprising about 40% of the circumference of the shaft and of sufficient length to overlap the two femoral fragments or the upper fragment and the upper end of the tibia if the entire lower end of the femur has been excised. They are placed in contact or embedded in the shorter fragment and anchored with two or three screws across the defect. If more than 10 cm. of the femur has been removed, it is usually necessary to take a graft from each tibia. If the tibia is resected for sarcoma, two grafts of equal dimensions should be used to repair the defect. A Kuntscher nail may be utilized. Defects of the humerus should be similarly repaired with two grafts from the tibia. On the other hand, a single graft from the tibia is all that is required for repair of a defect of the radius or ulna. Fresh homogenous grafts and bone bank grafts may be used with some success for the repair of defects created by excision of bone sarcoma; but fresh autogenous grafts are more biological and should not be abandoned for homogenous grafts except when the former are not to be had. Recent experiments on dogs have shown that when a 5 cm. segment of shaft of the tibia is resected and the defect repaired immediately by transplantation of a 5 cm. segment of tibia from various sources and fixation with a long intramedullary nail, the quickest and surest repair was obtained by the use of a fresh autogenous segment. Even the fresh homogenous segments were less satisfactory.

In case of small and medium-sized resections the repair is made at the time of the resection; but if several inches of the femur or tibia are removed, the transplantation of bone is postponed for 15 to 25 days, the limb being held in extension during the interval by a plaster dressing. A possible advantage might be gained if a segmental defect of the femur were filled with an accurately fitting segment of banked femur and rigidly fixed with a long Kuntscher intramedullary nail, thereby permitting the patient to be ambulatory during the long period of consolidation and reconstruction of the graft.

When defects are repaired with autogenous grafts as described, it is necessary to carry out immobilization by plaster dressings and metal splints for many months in

order to obtain bony union and creeping replacement of the necrotic bone by new bone.

There is little evidence that wide local resection or excision of a bone sarcoma, when performed under tourniquet constriction of the limb, is directly responsible for the development of distant metastases. On the contrary, the indications are that patients in whom demonstrable metastases have appeared after resection or amputation harbored unrecognizable metastases before operation. However, there has been local recurrence in a minority of cases treated by resection, and the percentage has been somewhat higher than that of recurrence in the stump when patients have been treated by amputation. It should be remembered in case of local recurrence following resection of a bone sarcoma that amputation may then be indicated, if there are still no demonstrable metastases, and the patient should be told so before operation.

Further support for resection of certain bone sarcomas of the extremities is to be found in the relatively large number of successes that have been realized from wide excision in similarly selected cases of sarcoma of the soft parts of the trunk, the extremities, and other parts of the body.

In view of the present advanced state of knowledge of bone sarcomas, the frequency with which they are diagnosed at an early stage and the improvement in the techniques of radical removal of diseased parts and of bone grafting for the repair of skeletal defects, it may be fairly concluded that an appreciable percentage of the sarcomas of the extremity bones now being amputated should be treated by resection and bone transplantation.

DALLAS B. PHEMISTER, M.D.

SYMPOSIUM ON PLASMA VOLUME EXPANDERS IN THE TREATMENT OF SHOCK

VOLEMIC SUBSTANCES FOR REPLACEMENT OF BLOOD

JESSE L. BOLLMAN, M.D.
ROBERT C. KNUTSON, M.D.
AND
JOHN S. LUNDY, M.D.
ROCHESTER, MINN.

SOLUTIONS of macromolecular substances have been used for the purpose of expanding the volume of plasma by virtue of their colloidal osmotic activity while they remain in the blood. Because of the large size of their molecules, their diffusion from the blood is correspondingly reduced and their colloidal effectiveness prolonged. It is obvious that such substances do diffuse rather rapidly into the extravascular fluids and some are sequestered in specific tissue spaces. The rapid decline of their concentration in the blood after intravenous injection indicates that considerable portions have left the blood within a few minutes. Grotte, Knutson and Bollman [1] found that dextran injected intravenously rapidly appeared in the lymph and that the colloidal osmotic gradient between the dextran in the blood and that in the extravascular fluids appear to be rapidly dissipated. The clinical effectiveness of these substances,[2] however, appears to be more prolonged than would be anticipated from the rapid rate of their equilibration with extravascular fluid. It is probable that the restitution of plasma volume immediately after administration of such substances enables the vascular system to regain its tone so that pressure and volume of blood may be maintained after the colloidal osmotic gradient of the substance used to expand the volume has become greatly reduced. It also may be

---

Dr. Bollman is from the Division of Experimental Medicine, Dr. Knutson is a Fellow in Anesthesiology, Mayo Foundation, and Dr. Lundy is from the Section on Anesthesiology, Mayo Clinic.

Read before the Section on Anesthesiology as part of a symposium on Plasma Volume Expanders in the Treatment of Shock at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

1. Grotte, G.; Knutson, R. C., and Bollman, J. L.: The Diffusion of Dextrans of Different Molecular Sizes to Lymph and Urine, unpublished data.

2. Lundy, J. S.; Gray, H. K., and Craig, W. McK.: Dextran in Supportive Therapy, with Comments on Periston and Gelatin, Arch. Surg. **61**:55-60 (July) 1950. Thorsén, Gunnar: Dextran as a Plasma Substitute, Lancet **1**:132-134 (Jan. 22) 1949. Fletcher, A. G., Jr.; Hardy, J. D.; Riegel, C., and Koop, C. E.: Gelatin as a Plasma Substitute: The Effects of Intravenous Infusion of Gelatin on Cardiac Output and Other Aspects of the Circulation of Normal Persons, of Chronically Ill Patients, and of Normal Volunteers Subjected to Large Hemorrhage, J. Clin. Invest. **24**:405-415 (July) 1945. Seldon, T. H.; Lundy, J. S.; Adams, R. C., and Cook, E. N.: Parenteral Administration of Gelatin, Proc. Staff Meet., Mayo Clin. **20**:468-469 (Nov. 28) 1945. Lundy, J. S.: New Solutions, Minnesota Med. **34**:21-23 (Jan.) 1951; Balanced Supportive Therapy During Anesthesia, Northwest Med. **50**:341-343 (May) 1951.

that the diffusion of these expanding substances into the extravascular fluids alters the fluids so that they are more available for maintenance of the volume of the circulating blood.

In our experiments we have attempted to determine the relative effectiveness of dextran, polyvinylpyrrolidone and solutions of gelatin and acacia for restoration of blood volume after hemorrhage produced experimentally. We found that each of these substances in proper concentration and volume was approximately as effective in the restoration and maintenance of the blood volume as was whole blood or plasma. Injection of saline solution of twice the volume of blood removed produced only slight effects on the blood volume as compared to the injection of one volume of macromolecular solutions. The addition of more fluid volume or saline solution to the macromolecular solutions further enhanced their effects.

METHODS

Adult rabbits which had had free access to food and water were anesthetized with ether and a small plastic tube was inserted into the femoral artery. The animals were then placed in a confining cage. Approximately an hour after operation, when the animals had recovered from the effects of the anesthetic, the clamp on the tube from the femoral artery was released and 20 ml. of blood for each kilogram of body weight was rapidly withdrawn. At this time exactly 2 ml. of a saline suspension of rabbit erythrocytes labeled with P^{32} was injected into the marginal vein of the rabbit's ear. Three minutes later approximately 1 ml. of blood was withdrawn from the arterial cannula after the stasis blood of the cannula had been discarded. Samples of blood for hematocrit readings by the Van Allen[3] method also were taken in this manner and were obtained at subsequent intervals of 15, 30 and 60 minutes, and 2, 3, 6 and 24 hours. Immediately after withdrawal of the three-minute sample of blood used to determine the volume, the substance used to expand the volume was injected as rapidly as possible into the femoral artery by way of the indwelling plastic tubes. Blood volumes were calculated from the measured dilution of radioactivity of the P^{32}-labeled erythrocytes and relative volumes of plasma and erythrocytes were determined from hematocrit readings, with the proper allowances for the amount of blood withdrawn from the animal. In most experiments the blood volume by the dilution method was determined only once and subsequent calculations from hematocrit readings were reverted to this determination. This method seemed valid because in other experiments similar figures were obtained when the blood volume was determined at more than one interval by the P^{32} method,[4] the Evans blue dye (T-1824) method,[5] and the iodinated I^{131} albumin method.[6]

RESULTS

Bleeding rabbits 20 ml. for each kilogram of body weight reduced the total of volume circulating blood to about 60% of its original value. With no subsequent treatment, the plasma volume increased rather gradually so that at the end of three hours the total blood volume approached 75% of its original value and great changes were not observed during the next 21 hours. At this time, however, it was found

3. Van Allen, C. M.: An Hematocrit Method, J. Lab. & Clin. Med. **10**:1027-1040 (Sept.) 1925.

4. Nylin, G.: Blood Volume Determinations with Radioactive Phosphorus, Brit. Heart J. **7**:81-84 (Apr.) 1945.

5. Gibson, J. G., Jr., and Evans, W. A., Jr.: Clinical Studies of Blood Volume: I. Clinical Application of a Method Employing the Azo Dye "Evans Blue" and the Spectrophotometer, J. Clin. Invest. **16**:301-316 (May) 1937.

6. Krieger, H.; Storaasli, J. P.; Friedell, H. L., and Holden, W. D.: A Comparative Study of Blood Volume in Dogs, Proc. Soc. Exper. Biol. & Med. **68**:511-515 (July-Aug.) 1948.

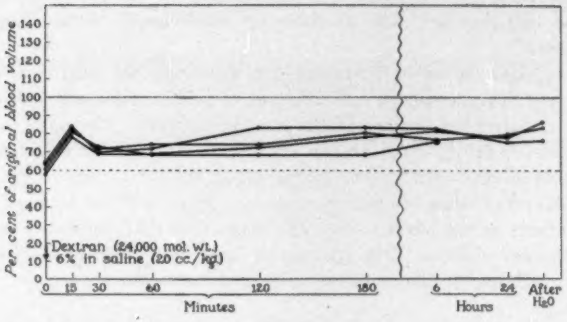

Fig. 1.—Blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate (time 0) replacement with an equal volume of 6% dextran (molecular weight, 24,000) in saline solution.

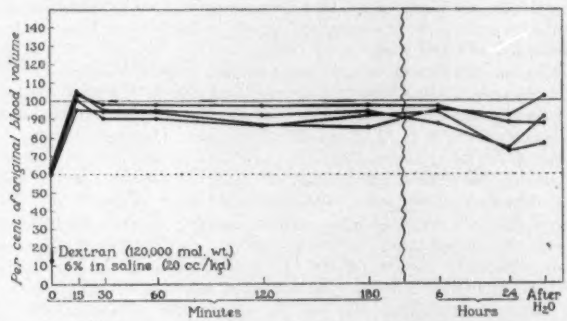

Fig. 2.—Blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection (time 0) of an equal volume of 6% dextran (molecular weight, 120,000) in saline solution.

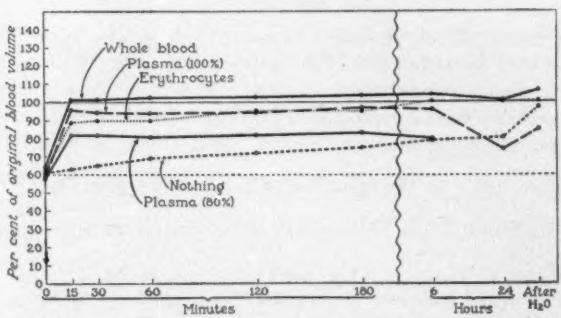

Fig. 3.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection (time 0) of an equal volume of whole blood, plasma, 80% plasma and erythrocyte suspension and after nothing was injected.

that the oral administration of 20 ml. of water for each kilogram of body weight caused, within the next half hour, an additional rise in the blood volume of about 10%. Approximately half of the animals which were bled but untreated died, usually between 6 and 24 hours after bleeding; no correlation was apparent, however, between the survival of the animals and their measured blood volume. The average blood volume of four untreated rabbits is shown in Figure 3.

The injection of a solution of 0.87% sodium chloride, after the removal of 20 ml. of blood for each kilogram of body weight, increased the blood volume immediately. Fifteen minutes after injection the blood volume was increased to approximately 70% of its original value, and in the next 24 hours the volume rose slightly to about 80% of the normal value. In general, the curves did not differ from those of the untreated bled animals except that higher values were indicated during the first hour after injection of saline solution. The average blood volumes of four rabbits after bleeding and replacement with an equal volume of saline solution are shown in Figure 9. The curves for average blood volume of four rabbits which

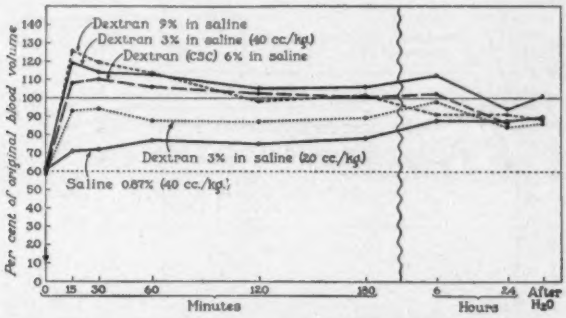

Fig. 4.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection (time 0) of equal volumes of 3% dextran, 6% dextran, 9% dextran and twice the volume of saline solution and of 3% dextran.

received 40 ml. of saline solution for each kilogram of body weight after withdrawal of 20 ml. of whole blood (Fig. 4) do not differ appreciably from those for rabbits which received only 20 ml. of saline solution. Curves for blood volume of the control group of rabbits which were untreated, although exposed to the same operative procedures, fasting and cage confinement, did not show appreciable deviation from curves for the original blood volume for 24 hours. Likewise, an injection of whole blood equal in amount to the 20 ml. for each kilogram of body weight which was withdrawn restored the original blood volume, and appreciable deviations from the original volume were not observed during the next 24 hours (Fig. 3). The injection of citrated plasma (20 ml. of plasma plus 5 ml. of citrate solution) after bleeding 20 ml. for each kilogram of body weight increased the plasma volume so that the blood volume remained at approximately 95% of its original value for six hours and subsequently decreased to about 75% during the next 18 hours (Fig. 3). When rabbit plasma (16 ml. of plasma plus 4 ml. of citrate) replaced the blood withdrawn, the blood volume was maintained at about 80% of

its original value (Fig. 3). Replacement of the erythrocytes withdrawn, washed and suspended in saline solution increased the blood volume to about 90% of its original value, and it remained essentially unchanged for the next 24 hours (Fig. 3).

A dextran fraction, obtained after partial hydrolysis and precipitation by increasing concentrations of ethyl alcohol[7] so that the resulting product had a molecular weight of 24,000, was used in 6% solution in saline solution to replace an equal volume of blood withdrawn. The resultant curves for blood volume were essentially similar to those observed when saline solution alone was injected (Fig. 1). Injection of similar volumes of dextran of 120,000 molecular weight, however, returned the blood volume to its original level, which fell only slightly during the next 24 hours (Fig. 2).

In six rabbits replacement of blood withdrawn by an equal volume of a 6% solution of dextran in saline solution, 20 ml. for each kilogram of body weight, was followed by an immediate rise in blood volume to about 110% of its original value. The blood volume returned to approximately normal in about two hours and remained unchanged for the next 22 hours (Fig. 4). Similar replacement of the

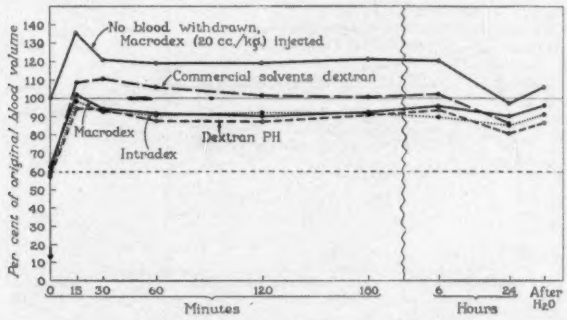

Fig. 5.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection (time 0) of equal volumes of 6% dextran from different sources.

withdrawn blood by a 3% solution of dextran in saline solution increased the blood volume to about its original value. Within the next hour the blood volume declined to about 90% of its original volume and remained essentially unchanged for the next 23 hours. A somewhat greater increase in blood volume was obtained after the replacement of blood withdrawn, 20 ml. for each kilogram of body weight, with 40 ml. of 3% solution of dextran in saline solution. For the next 24 hours the blood volume remained slightly more than its original value. Replacement of equal volumes of blood withdrawn with 9% solution of dextran in saline solution increased the blood volume to about 125% of its original value; it declined to its original volume in about two hours, with little subsequent change during the next 22 hours (Fig. 4). In rabbits which were similarly treated but not bled, the injection of a 6% solution of dextran in saline solution, 20 ml. for each kilogram of body weight, produced an immediate marked increase in the blood volume, which declined to

7. Ingelman, B., and Halling, M. S.: Some Physico-Chemical Experiments on Fractions of Dextran, Arkiv. Kemi **1**:61-80, 1949.

about 120% of the original volume within 30 minutes and remained unchanged for six hours. Twenty-four hours after the injection the blood volume was approximately at its original level (Fig. 5).

Replacement of blood withdrawn with equal volumes of a solution of 6% dextran from different manufacturers produced essentially the same response of the blood volume. The average curves from four rabbits, each of which received equal volumes of dextran Ph, macrodex (Sweden), intradex (England) and dextran (United States), are shown in Figure 5.

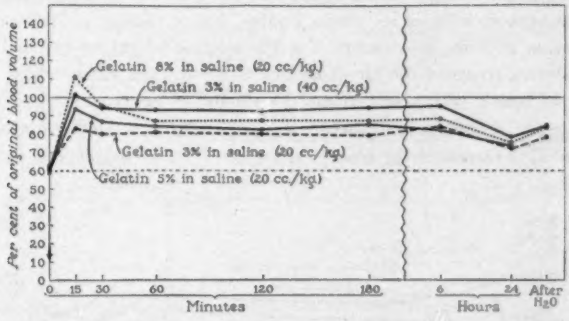
Per cent of original blood volume
Gelatin 8% in saline (20 cc./kg.)
Gelatin 3% in saline (40 cc./kg.)
Gelatin 3% in saline (20 cc./kg.)
Gelatin 5% in saline (20 cc./kg.)
Minutes
Hours
After H2O

Fig. 6.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection (time 0) of equal volumes of 3, 5, and 8% gelatin in saline solution and twice the volume of the 3% gelatin solution.

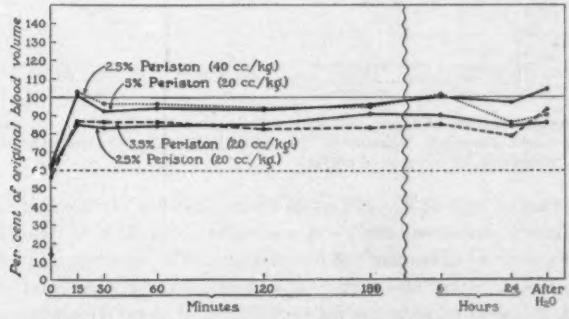

Fig. 7.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection of equal volumes of 2.5, 3.5, and 5% polyvinylpyrrolidone (periston) in saline solution and twice the volume of 2.5% polyvinylpyrrolidone.

The injection of equal volumes of 3.5% solutions of polyvinylpyrrolidone in saline solution, after bleeding 20 ml. for each kilogram of body weight, increased the blood volume to about 85% of its original value and maintained the blood volume near this level for 24 hours. Similar injections of 2.5% solutions of polyvinylpyrrolidone increased the blood volume almost as much; injections of the same volume of 5% solutions of polyvinylpyrrolidone, or twice the volume of 2.5% solution, increased and maintained the blood volume at about 95% of its original value (Fig. 7).

The replacement of blood withdrawn by equal volumes of an 8% solution of gelatin in saline solution, 20 ml. for each kilogram of body weight, increased the blood volume to 110% of its original value, but within an hour the volume declined to 85% and remained constant for six hours, with a further decline to 75% after 24 hours. Replacement of the blood lost by a 6% solution of gelatin increased the blood volume to its original level, but subsequently it declined to 90% at six hours and 70% at 24 hours. Injection of a 5% solution of gelatin under similar circumstances altered the blood volume to about the same extent. The replacement of the blood lost by equal volumes of a 3% solution of gelatin in saline solution increased the blood volume to 85% of its original value, with a decline to 70% at 24 hours. Administration of twice the volume of a 3% solution of gelatin for each 20 ml. of blood withdrawn returned the blood volume to its original value, which was maintained for six hours, with a subsequent decline for 24 hours to 80% (Fig. 6).

Replacement of blood withdrawn by an equal volume of a 9% solution of acacia in saline solution increased the blood volume to 105% of its original value, with a

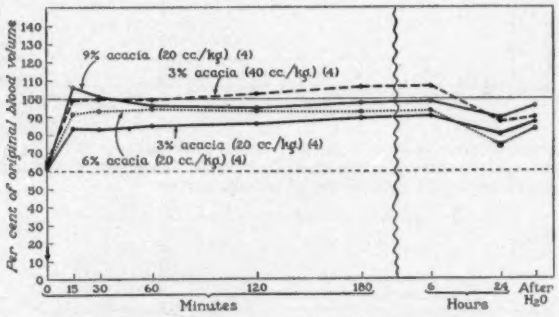

Fig. 8.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate injection of 3, 6, and 9% solutions of acacia in saline solution and twice the volume of 3% solution of acacia.

gradual decline to 90% at the end of 24 hours. Similar replacement with a 6% solution of acacia maintained the blood volume at about 90% of its original value for six hours, with a subsequent fall for 24 hours. The injection of a 3% solution of acacia in the same way was slightly less effective, and the injection of twice the volume of a 3% solution of acacia for each 20 ml. of blood withdrawn maintained the original blood volume for six hours, with a subsequent fall to 85% after 24 hours (Fig. 8). The average curves for blood volume of rabbits after bleeding 20 ml. for each kilogram of body weight and the immediate replacement with equal volumes of saline solution or solutions containing 6% dextran, 6% gelatin, 6% acacia and 3.5% polyvinylpyrrolidone are shown in Figure 9.

Dextran appears to be about as effective in the replacement of blood volume in dogs as in rabbits. In our experiments dogs were prepared in a manner similar to that employed for rabbits, and 20 ml. of blood for each kilogram of body weight was withdrawn soon after the animals had recovered from the ether used during the surgical procedure. The curves for the blood volume of dogs which received

equal volumes of a 6% solution of dextran for the blood withdrawn are given in Figure 10. In our hands, rats did not seem to be suitable animals for this bleeding and reinjection procedure. Rats from which blood was withdrawn in amounts of 25 ml. for each kilogram of body weight usually underwent some degree of collapse, which was not always relieved by immediate injection of equal amounts of whole blood or plasma or by injection of saline solution or dextran. The injection of a 6% solution of dextran, equal in volume to the blood withdrawn, appeared definitely more detrimental to the rat than if no injection had been made. Our determinations for blood volume were not as consistent as those obtained with rabbits and dogs,

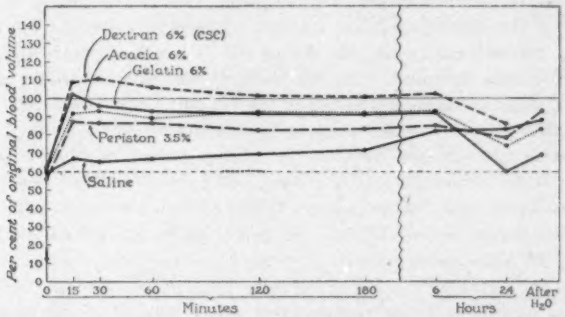

Fig. 9.—Average curves of blood volume of rabbits after bleeding 20 cc. for each kilogram of body weight and immediate replacement of equal volumes of saline solution and solutions containing 6% dextran, 6% gelatin, 6% acacia and 3.5% polyvinylpyrrolidone.

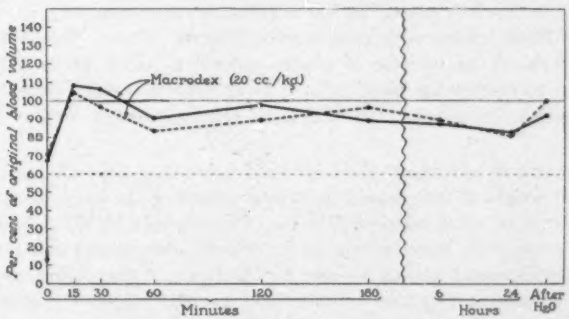

Fig. 10.—Blood volume of dogs after bleeding 20 cc. for each kilogram of body weight and immediate injection (time 0) of an equal volume of 6% dextran in saline solution.

but the volume of plasma of the rat usually rose from about 60% of its original volume after bleeding to 80 or 90% within an hour without any intravenous replacement of the fluid lost. The reinjection of whole blood or plasma returned the blood volume to its original value, but inconsistent results were obtained after injections of dextran. The state of collapse of the bled rats did not appear to be directly related to the restoration of blood volume by whole blood or other substances which we injected.

COMMENT

These experiments were designed primarily to check the efficacy of several macromolecular substances for the maintenance of blood volume after acute loss of blood. We hoped to be able to avoid any secondary alterations in blood pressure and permeability which might arise after the experimental procedures. The steady maintenance of the original volume of blood after the experimental regimen and replacement with blood of blood withdrawn indicated that secondary factors were not producing appreciable changes. In all experiments in which the whole blood was not replaced definite changes in the volumes of blood and plasma occurred which were not the result of simple addition of the injected fluid to the volume of circulating blood. When the withdrawn blood was not replaced by injection, the erythrocyte volume did not increase appreciably during the 24 hours of observation, but 50 to 60% of the plasma volume lost by the bleeding was restored within three hours, with only a slight subsequent increase in the next 21 hours. After the reinjection of the erythrocytes with saline solution substituted for plasma, more than 40% of the solution had diffused from the circulating plasma within 15 minutes, but within two hours almost all loss of plasma volume was restored and the original volume was maintained. When saline solution was used to replace the blood lost, about 75% of the saline injected had diffused from the plasma within 15 minutes, and within six hours more than 80% of the plasma volume lost by bleeding was restored. The controlled conditions of these experiments are that after bleeding the erythrocyte volume is not replaced but nearly 60% of the plasma volume is replaced in about three hours; when saline solution is used about 80% of the plasma volume is replaced at the same time. The loss of red cells does not appear to be a major factor in the restoration of plasma volume, but of course the loss is apparent in the volume of whole blood. In our experiments approximately 15 of the 40% of the total blood volume withdrawn was erythrocyte volume. Unless the erythrocytes are replaced, an increase of plasma volume to 125% of its original value is necessary to restore the blood volume to its original value. When the plasma volume has its original value, the total blood is approximately 85% of its original volume.

Replacement of withdrawn blood by equal volumes of 6% solutions of dextran of molecular weight 24,000 showed no greater effects on the blood volume than did similar amounts of saline solution. The use of dextran of 120,000 molecular weight, however, restored the blood volume to its original volume and maintained a correspondingly increased plasma volume for 24 hours. Other solutions of macromolecular substances prepared commercially for the purpose of expanding the volume of plasma, that is, dextran, polyvinylpyrrolidone, gelatin and acacia, were likewise effective in replacing the volume of blood. Dextran and polyvinylpyrrolidone appear to remain effective somewhat longer than do solutions containing gelatin or acacia under the same conditions.

It is obvious in all our experiments that the volume of fluid available bears some relationship to blood volume. In all experiments, more fluid was retained when an equal amount of saline solution was given with the volume-expanding solution. Hypertonic macromolecular solutions were more effective immediately than was the additional volume of saline solution with more dilute solution, but this advantage was soon lost. These observations, however, do suggest that the concentration and

amount of substances administered to expand the volume could well be varied to produce the effects desired, that is, larger amounts of more dilute solutions could be used in cases in which hydration of the blood and body tissues is desired and smaller amounts of more concentrated solutions if hydration of the blood and dehydration of the tissues are required.

These macromolecular substances are effective in increasing the plasma volume owing to their colloidal osmotic effect for the short time that they remain in the blood in greater concentration than is present in the extravascular fluid. Diffusion of dextran and presumably other macromolecular substances into the lymph is rapid, and the sustained action of these substances appears to be the result of changes which they produce in the extravascular fluids as well as of their retention in the blood.

SUMMARY

Several macromolecular substances, when injected intravenously immediately after bleeding, are effective in replacing the volume of blood after measured amounts of hemorrhage. The extent and duration of the increase in blood volume are directly related to the amount of the substances administered, provided that the molecular size is sufficient to prevent rapid elimination. The volume of fluid administered is equilibrated with the blood and tissue fluids with extreme rapidity, and the sustained increases of blood volume thus obtained are dependent on the degree of hydration of the extravascular tissues as well as that of the blood. The presence of macromolecular substances in the extravascular fluids appears to aid in the maintenance of volume of blood after hemorrhage.

TISSUE CHANGES FOLLOWING THE USE OF PLASMA SUBSTITUTES

FRANK W. HARTMAN, M.D.
DETROIT

RENEWED interest in plasma substitutes or plasma extenders and emergency substances has been brought about by the apparently successful production and use of dextran and polyvinylpyrrolidone abroad, the favorable impression made by their trial here, as outlined in the previous communication, and most important, the definite need for supplies of this type which may be stock-piled in large quantities for indefinite periods against major disasters.

It is now well established that certain exogenous as well as endogenous macromolecular colloids are capable of increasing and maintaining blood volume by means of their osmotic pressure, hydrophilic properties and slow elimination from the vascular system. It is the purpose of this communication to evaluate the pathologic tissue changes resulting from the introduction of these colloids rather than their physiologic effects or their effectiveness in shock and dehydration. As outlined by Hueper [1] and others,[2] the four exogenous macromolecular substances now most available as plasma extenders fall into the following chemical groups: (1) proteins, (2) carbohydrates, and (3) synthetics. These groups are represented at the present time by the following substances: gelatin, dextran and pectin, and polyvinylpyrrolidone (PVP), all of which have had rather extensive experimental and clinical applications.

From the standpoint of pathologic tissue changes in the body following the administration of these colloidal solutions, it is felt that the following criteria should apply: 1. The normal number and function of the formed elements of the blood should be maintained. 2. Sludging of the blood with predisposition to thrombosis and embolism should be minimized. 3. Rapid accumulation of the colloids in organs or tissues sufficient to interfere with function should be avoided. 4. Prolonged retention of the injected material in vital tissues or organs contraindicates the use of that material. 5. The material should be at least partially metabolized in the body.

Read before the Section on Anesthesiology as part of a symposium on Plasma Volume Expanders in the Treatment of Shock at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

1. Hueper, W. C.: (*a*) Macromolecular Substances as Pathogenic Agents, Arch. Path. **33**:267, (Feb.) 1942; (*b*) Experimental Studies on Cardiovascular Pathology: Effects of Intravenous Injections of Solutions of Gum Arabic, Egg Albumin and Gelatin upon the Blood and Organs of Dogs and Rabbits, Am. J. Path. **18**:895, 1942.

2. Popper, H.; Volk, B. W.; Meyer, K. A.; Kozoll, D. D., and Steigman, F.: Evaluation of Gelatin and Pectin Solutions as Substitutes for Plasma in the Treatment of Shock, Arch. Surg. **50**:34, (Jan.) 1945. Richter, G. W.: Parenchymatous Lesions of Liver and Kidney of Mice Due to Pectin, Am. J. Path. **26**:379, 1950.

Of the compounds under consideration, gelatin has a molecular weight of about 150,000, dextran 300,000, and pectin 250,000 previous to degradation. All have not only large molecules but also long, rod-shaped or chain-like configurations giving a length many times their diameters, roughly resembling fibrinogen rather than the spheroid outline of albumin or globulin, which is desirable if these colloids are to resemble plasma in physical properties.

Because of both the large size and the different configuration of the molecules, it becomes necessary to degrade or polymerize all the compounds under consideration in order to approach the size and dimensions of the molecule of albumin or globulin. This is readily accomplished with heat, but the resulting substance is a mixture of small, medium and large molecules in which only the average size compares with the desirable 50,000 to 80,000 molecular size of most plasma proteins. Even the degradation does not change the shape of the molecule, but perhaps with the method suggested by Pauling for the treatment of gelatin, the smaller elongated molecules of the degraded chemical can be grouped into roughly spheroid bundles.

Of the substances under consideration, none has been shown to be metabolized in the body. All are eliminated from the circulation by the kidneys with relative rapidity in amounts up to 70 to 80%. The remaining portions are eliminated more slowly, but actual evidence of metabolism is lacking. Not only are the compounds not metabolized, but they are actually inert and are phagocytized by the reticuloendothelial cells and infiltrate the endothelium of blood vessels as well as the parenchymal cells of the various tissues and organs. Hueper[1a] observed that with increasing accumulation of macromolecular substances in the cells escape is difficult unless cell membranes become defective through degeneration or necrosis. There is both experimental and clinical evidence that the body is capable of removing macromolecular material so long as the deposit is not large and does not seriously interfere with function of the cell or organ affected. The storage of macromolecular material occurs in the reticuloendothelial cells of the liver, spleen and lymph nodes, the endothelial cells of blood vessels and the parenchymal cells of various organs, particularly the liver, kidney and brain.

I. TISSUE CHANGES FOLLOWING THE ADMINISTRATION OF GELATIN

The gelatin used was that prepared for general clinical use by Sharp & Dohme, Inc., and was a 6% solution of the osseous variety. Oxypolygel, prepared by the Pauling method,[3] was not available for study.

Although many articles dealing with the effect of gelatin administered intravenously have been published, the recent contribution of Skinsnes[4] based on a postmortem study of 23 patients receiving this type of therapy is probably the most pertinent in regard to tissue changes. His findings show that, grossly, the kidneys are swollen and the cut surfaces tend to bulge and the average weight is 210 gm. "Microscopically the lesions are similar to those described for sucrose nephrosis. . . . The epithelial cells of the proximal convoluted tubules present a granular, finely vacuolated swelling, often so severe that the tubular lumens are evident only

3. Campbell, D. H.; Koepfli, J. B.; Pauling, L.; Abrahamsen, N.; Dandliker, W.; Feizen, G.; Lanni, F., and LeRosen, A.: Conference on Blood Substitutes, Appendix D, p. 73, National Research Council Bulletin, 1949.

4. Skinsnes, O. K.: Gelatin Nephrosis: Renal Tissue Changes in Man Resulting from the Intravenous Administration of Gelatin, Surg., Gynec. & Obst. 85:563, 1947.

as slits." In regard to the duration of this "gelatin nephrosis," no lesions were found when 120 hours had elapsed between the administration and the autopsy.

In our work 50 mice were given seven intravenous injections of 1.8 gm. per kilogram over a period of 21 days. The tissue changes in mice were comparable to those described by Skinsnes [4] in human beings. The gelatin nephrosis produced was of short duration.

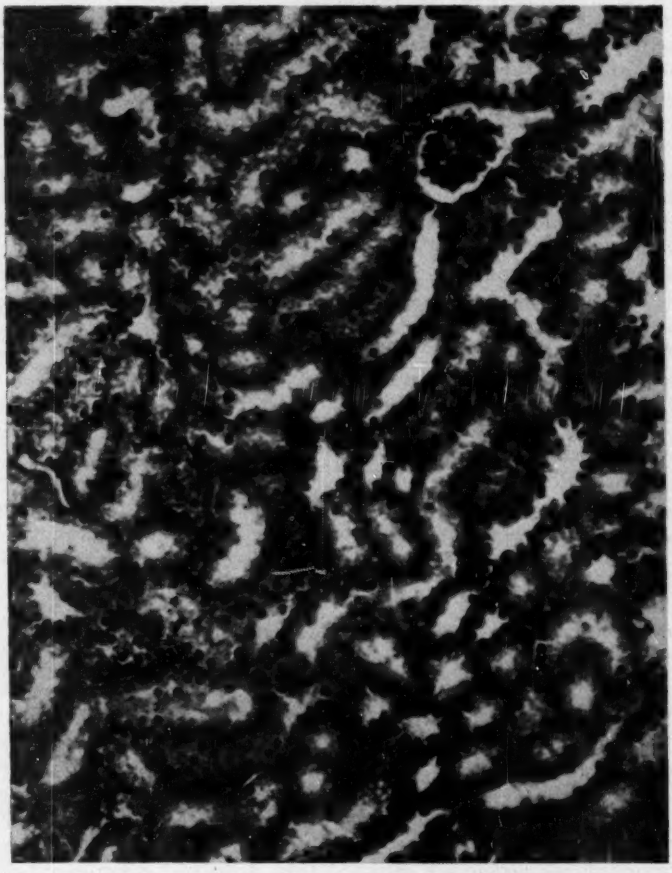

Fig. 1.—Medium-power photomicrograph of kidney after administration of gelatin showing swelling and vacuolation of tubular epithelium.

II. TISSUE CHANGES FOLLOWING THE ADMINISTRATION OF DEXTRAN

Although abundant publications regarding the use of dextran in human beings appears in the Swedish and English literature, only two recent articles on the application to experimental animals appear in American journals.

The first is that of Goldenberg, Crane and Popper [5] presenting experiments on rabbits and dogs using macrose, a 6% partly hydrolyzed dextran in distilled water prepared by the Schenley Laboratories. Their animals received 15 cc. per kilogram three times weekly for as many as 46 injections. As regards tissue changes, the kidneys were most affected. Marked vacuolization of the tubular epithelium and dilata-

Fig. 2.—High-power photomicrograph of kidney after administration of gelatin showing nephrotic tubules with swelling and cast formation.

tion of the lumen were found, especially in the proximal and distal convoluted tubules. Further homogeneous pink-staining swelling of the glomerular loop appeared. In a few instances pink-staining material appeared in the interstitial tissue near the corticomedullary border. The lesion is spoken of as a nephrosis comparable

5. Goldenberg, M.; Crane, R. D., and Popper, H.: Effect of Intravenous Administration of Dextran, a Macromolecular Carbohydrate, in Animals, Am. J. Clin. Path. **17**:939, 1947.

to that associated with sucrose and gelatin administrations, since no impairment of renal function was encountered.

The second contribution is that of Nelson and Lusky,[6] in which 10 cc. per kilogram of 6% dextran (macrodex) was given to rabbits in each of 16 intravenous injections over a two-month period. It is stated that very little effect in the tissues was found.

In our work dextran, kindly supplied by Chemical Solvents Corporation, was used in 6% solution, 1.8 gm. per kilogram being given every third day for seven injections intravenously in 50 mice.

Fig. 3.—Medium-power photomicrograph of lymph gland after administration of dextran showing foam-cell formation.

The retention in the tissues was marked, involving the lymph nodes, liver, kidneys, and blood vessels. The foam-cell production in lymph nodes is striking. The liver cells demonstrate granular and vacuolar changes. The kidneys show the

6. Nelson, A. A., and Lusky, L. M.: Pathological Changes in Rabbits from Repeated Intravenous Injections of Periston (Polyvinyl Pyrrolidone) or Dextran, Proc. Soc. Exper. Biol. & Med. **76**:765, 1951.

swelling and vacuolization and desquamation of the epithelium of the proximal convoluted tubules. The blood vessel walls, especially in the lung, show infiltration with foam cells and in a few cases rupture. Most of these changes are reversible, but nephrosis and the blood vessel involvement need further study.

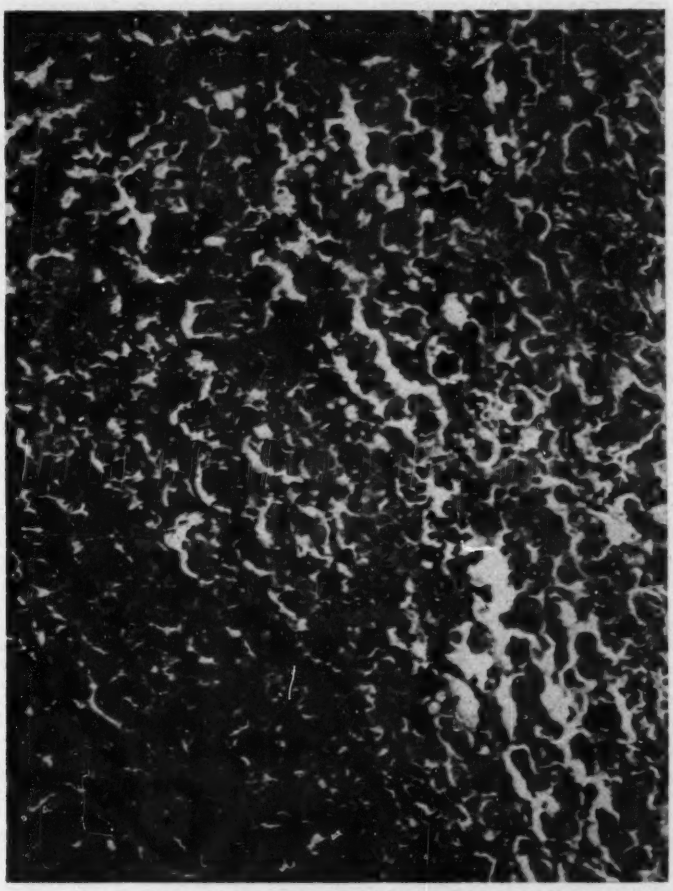

Fig. 4.—Medium-power photomicrograph of lung after administration of dextran showing infiltration of foamy phagocytic cells.

III. TISSUE CHANGES FOLLOWING THE ADMINISTRATION OF PECTIN

The use of partially hydrolyzed pectin solutions as a plasma substitute was reported earlier by Hartman and others.[7] The solutions used were degraded at first

7. Hartman, F. W.; Schelling, V.; Harkins, H., and Brush, B.: Pectin Solution as a Blood Substitute, Ann. Surg. **114**:212, 1941. Hartman, F. W.; Schelling, V.; Harkins, H.;

(Footnote continued on next page)

by autoclaving but later by prolonged exposures to a temperature of 212 F. With these carefully degraded solutions, 70% of the pectin was excreted in the first 24 hours, and no permanent storage was found in either dogs or patients. In 1942, Hueper [18] tried both raw and autoclaved pectin solutions in experimental animals.

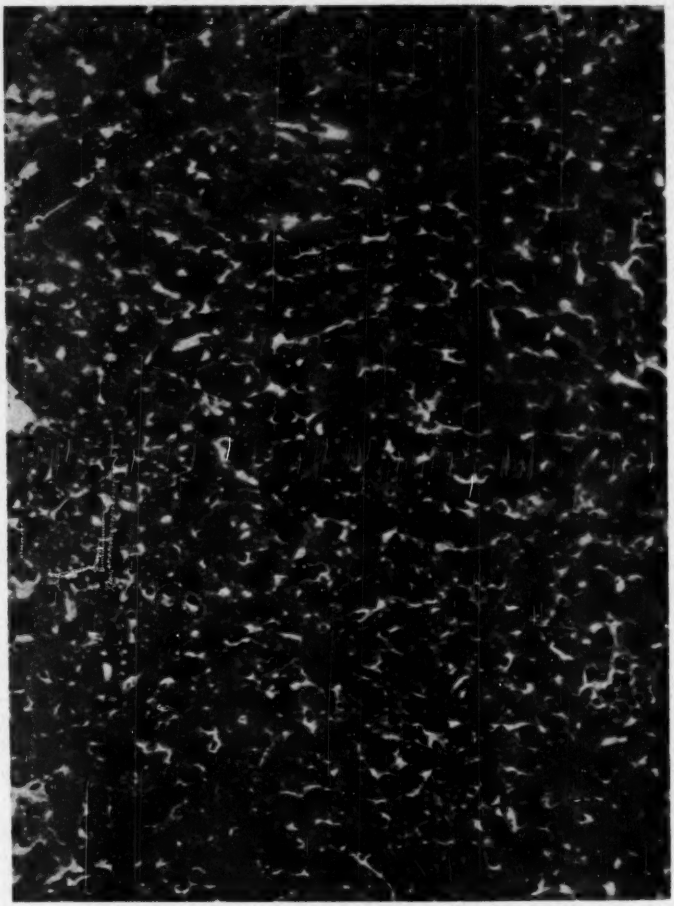

Fig. 5.—Medium-power photomicrograph of liver after administration of pectin showing moderate acute retention in liver cells.

Brush, B., and Warren, K. W.: Blood Substitutes, brochure in Connection with Scientific Exhibit on Pectin Solutions in the Treatment of Shock, at the Ninety-Third Annual Session of the American Medical Association Atlantic City, June, 1942. Hartman, F. W.; Schelling, V.; Brush, B., and Warren, K. W.: The Relative Value of Pectin Solution in Shock, J. A. M. A. **121**:1337 (April 24) 1943.

With the first group receiving raw pectin, the typical storage phenomena were found, but, he states, "dogs and rabbits given injections of autoclaved pectin solution showed on the other hand, with the exception of one rabbit, only minor storage phenomena in the bone marrow and foci of hyaline degeneration and thickening of the arteries . . . These differences in degree and type of reaction are due to the fact that pectin solutions are markedly depolymerized when exposed to heat and lose thereby much of their macromolecular characteristics and their original physicochemical properties."

The solutions degraded at 212 F. for 24 hours were filtered through a Seitz bacterial pad, and the resulting material had molecular weights of 40 to 70,000 and kept without precipitation for several months. For convenience and to prevent further polymerization, sodium pectinate may be prepared from this material and kept in dry form. More recently the method of Pauling [8] for the degradation of gelatin has been used in the degradation of pectin.

One per cent pectin administered to 50 mice was prepared by the Pauling procedure. Each mouse received seven intravenous injections (0.3 gm. per kilogram per injection) over a 21-day period. Retention in the tissue was noted after the injection first in the reticuloendothelial cells of the lymph nodes, parenchymal cells of the liver, tubular epithelium of the kidneys, especially in the convoluted tubules, and to a less extent in the lungs and blood vessels. The animals allowed to live remained in good condition, and no significant storage appeared with the seven full injections.

IV. TISSUE CHANGES FOLLOWING THE ADMINISTRATION OF POLYVINYLPYRROLIDONE

There are many reports on polyvinylpyrrolidone in the German literature, for the most part on its clinical application. Those given here refer to tissue retention. Schallock,[8] after studying storage in 52 animals and 102 autopsies, found that the greater the relative amount of infused polyvinylpyrrolidone, the greater the danger of pathological reactions. Müller [9] reported that the appearance of the spleen and lymph nodes after polyvinylpyrrolidone injections was comparable to that in the storage diseases, while the liver and the bone marrow showed only slight changes. Schoen [10] noted accumulation of polyvinylpyrrolidone after injection in liver, spleen, lymph nodes and lungs. German army pathologists found damage in both liver and kidneys from polyvinylpyrrolidone and late in World War II advised use of lyophilyzed plasma.

One of the few observations in this country on the experimental use of polyvinylpyrrolidone is the recent one of Nelson and Lusky,[6] in which they describe their findings in rabbits receiving 16 injections of 10 cc. per kilogram of 3.5% solution of polyvinylpyrrolidone (periston) in distilled water over a 30-day period. Grossly, the spleen showed slight enlargement. Microscopically the principal lesion was

8. Schallock, G.: Anatomical Investigation of the Fate of Blood Substitutes in the Organism and the Reactions Caused Thereby, Beitr. path. **108**:405, 1943.

9. Müller, W.: Zur pathologischen Anatomie der alimentären Intoxikation, Deutsche med. Wchnschr. **71**:32, 1946.

10. Schoen, H.: Organveränderungen beim Säugling nach Zufuhr von Periston, Klin. Wchnschr. **27**:463, 1949.

foam-cell storage, noted most in the spleen. Tissues involved to a less extent were lymph nodes, bone marrow, adrenal medulla, liver, lungs and thymus.

For our work the polyvinylpyrrolidone (an imported brand) was kindly furnished by General Analine and Film Corporation. This material has an average molecular weight range of 20 to 80,000. Fifty mice were given seven injections of 3.5% polyvinylpyrrolidone (PVP) in isotonic sodium chloride solution, 1.05 mg.

Fig. 6.—Medium-power photomicrograph of lung after administration of polyvinylpyrrolidone showing endothelial cells of blood vessel vacuolated, swollen and extending into the lumen.

per kilogram over a three-week period. The material was well tolerated, and the animals remained in good condition. Foam cell formation was noted after the third injection in the lymph nodes. After the seventh injection retention was well marked in liver, kidneys, adrenals, bone marrow, lungs and blood vessels. The material appears as granules and vacuoles. No actual necrosis was found in the liver, but in

the kidney the tubular epithelium frequently desquamated to form cell casts. The changes in the blood vessels are perhaps the most significant, as most of the changes described by Hueper[11] resulting from the use of methylcellulose and polyvinyl alcohol are seen, that is, swelling and vacuolization of the endothelium with palisade formation, mural thrombus formation and rupture.

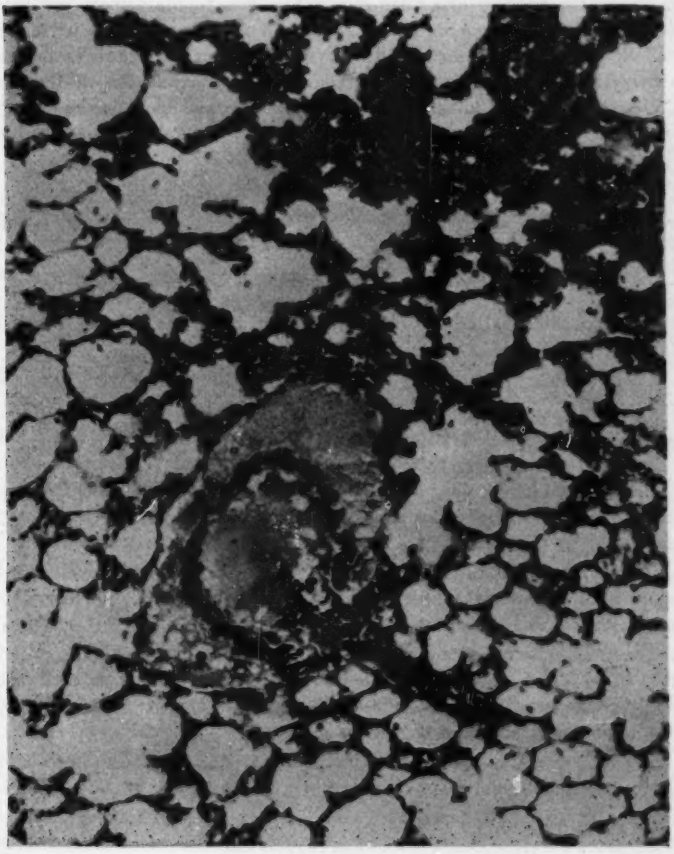

Fig. 7.—Medium-power photomicrograph of lung after administration of polyvinylpyrrolidone showing capillary wall infiltrated and ruptured.

COMMENT

It is evident from a review of the literature and the data presented that macromolecular substances which have osmotic pressures and hydrophilic properties comparable with those of blood plasma and hence are possible plasma substitutes or

11. Hueper, W. C.: Organic Lesions Produced by Polyvinyl Alcohol in Rats and Rabbits, Arch. Path. **28**:510, 1939.

extenders are all relatively inert chemically, are not metabolized in the body and, therefore, produce storage phenomena either acute, chronic, or both. Since these substances are inert and are not metabolized, their elimination from the body and chronic retention in the tissues seem to depend on their chemical stability and their molecular size, as best illustrated by the tissue changes due to raw and degraded pectin. The difficulties regarding molecular size have been partially, if not principally, due to the average molecular size rather than to the actual size. In other words, it is necessary to obtain the molecular size needed for osmotic pressures and hydrophilic properties and then produce that size through synthesis in the case of polyvinylpyrrolidone and through degradation and fractionation in the case of gelatin, dextran and pectin, thus eliminating the molecules too small to be effective and those so large that excretion is too slow and chronic retention becomes a possibility.

CONCLUSIONS

1. All macromolecular substances now available as blood substitutes—gelatin, dextran, pectin and polyvinylpyrrolidone—are eliminated from the body with relative rapidity if of proper molecular size.

2. With repeated or large intravenous injections, varying amounts are taken up by the reticuloendothelial cells, the endothelium of blood vessels, and, particularly, the parenchymal cells of liver and kidney.

3. There is acute retention of gelatin in the epithelium of the convoluted tubules of the kidney producing nephrosis, yet chronic storage is not encountered.

4. Dextran is rapidly stored, especially in the liver and the reticuloendothelial cells.

5. Pectin degraded by the Pauling method is stored rapidly in the liver, kidney and reticuloendothelial cells, but none has been found in blood vessels or bone marrow.

6. Polyvinylpyrrolidone (PVP) is stored rapidly and in larger quantities than gelatin, dextran or pectin. The endothelium of blood vessels, reticuloendothelial cells, liver, kidney and spleen are the principal sites.

7. The four substances under consideration as plasma extenders appear satisfactory in so far as acute tissue changes are concerned for use as emergency or prophylactic measures against shock states in the following order: gelatin, dextran, pectin, and polyvinylpyrrolidone.

8. The total dosage should be curtailed in any 24-hour period to prevent excessive retention which might favor chronic storage.

9. When one substance, such as gelatin, tends to embarrass a single organ, the kidney, a second substance such as dextran or pectin might be used alternately.

10. Further investigation should seek substances that can be utilized by the various cells and tissues (preferably contributing to nitrogen balance) without the hazard of storage.

PRESENT STATUS OF PLASMA VOLUME EXPANDERS IN THE TREATMENT OF SHOCK

Clinical Laboratory Studies

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SINCE many will find the investigative approach of our group somewhat unusual, I shall first attempt to elucidate the factors necessitating the procedure which we have followed. At the time we started our study on plasma volume expansion, certain unquestionable facts had been established. The first was that shock was frequently associated with decreased plasma volume and the second was that any substance which would expand and maintain plasma volume would often bring about relief of shock. The third established fact was the practical consideration that most of the substance used previously resulted in storage of the material in the body or in functional impairment of one or more organs.

To reach a solution in this problem it was necessary to find a substance which was capable of remaining in the blood stream, maintaining the vascular volume, and eventually being excreted or metabolized. Glycogen appeared to answer our demands, and our first studies were performed on this substance. However, the data on dextran indicating its structural relationship to glycogen and the ease with which dextran could be produced turned our attention to this substance. As a consequence, for the last two and a half years our attention has been directed toward the study of any hematopoietic, renal, hepatic or circulatory impairment which might occur as a result of the use of partially hydrolyzed dextran for injection. The studies were conducted first on patients who had normal function of the above mentioned systems and later on patients who had measurably reduced functional reserve at the time of the study. During this investigation the degree and duration of plasma volume expansion and the fate of the injected material were determined.

The major hematological findings of our studies are as follows: 1. The hematocrit falls as a result of hemodilution and returns to normal gradually. This determination bears an approximate inverse relation to the plasma volume expansion. 2. No difficulty was encountered in typing, cross matching, or Rh determination in 27 patients, 14 of whom were in shock. Dextran blood levels ranged from 421 to 3,000 mg. per 100 cc. in this group of patients. 3. The sedimentation rate

Read before the Section on Anesthesiology as part of a symposium on Plasma Volume Expanders in the Treatment of Shock at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

The data reported in this paper are the results of the efforts of a team of investigators of which the author was the responsible investigator on a contract from the United States Army. Detailed discussion of the individual problems in the paper will be presented elsewhere.

increases in relation to the amount of dextran in the blood and returns to normal as the dextran concentration diminishes. 4. Leukopenia is not observed, as might be expected from previous experience with macromolecular substances.

The evaluation of renal function was first made by the use of the usual clinical procedures. No microscopic findings or proteinuria was observed in the urine of patients after dextran administration. The specific gravity of urine is increased by the dextran excreted in the urine, and this change was noted only during the maximum dextran excretion (first six hours). The nonprotein nitrogen of the blood remains unaltered after the injection of dextran, and in 10 consecutive patients phenolsulfonphthalein determinations before and after dextran injection showed no change. Several of these patients have been restudied at six month intervals, and no change in renal function has been observed. In order to study renal function more precisely, paraaminohippurate and creatinine clearances have been studied in 10 patients. No change has been observed in either renal plasma flow or glomerular filtration rate after intravenous injection of 500 or 1,000 cc. of dextran. The absence of change in renal plasma flow is rather surprising, since albumin has been shown to alter renal plasma flow when comparable amounts are injected. A series of patients having proteinuria of varying degree have been given injections of 500 cc. of dextran. No change in the proteinuria resulted from the dextran administration.

Studies on the circulatory effects of dextran have been effected by means of cardiac catheter techniques. Cardiac output as determined by the dye dilution method indicates an approximate increase of 20% after injection of 500 cc. of dextran. This change results from an increased stroke volume. The peripheral venous pressure, right auricular pressure and pulmonary capillary pressure all increase, as might be expected from a sudden expansion of plasma volume. Vital capacity is unaltered as is the blood pressure. No changes have been observed in the electrocardiogram after dextran injection. Studies on the circulatory dynamics of a small series of patients from whom 500 to 800 cc. of blood has been removed and who have then been treated with 500 cc. of 6% hydrolyzed dextran indicate that after plasma volume replacement there is a return to normal levels.

Clinical tests usually associated with measurement of some phase of hepatic function, sulfobromophthalein retention, cephalin flocculation, thymol turbidity, icterus index, and total protein with albumin and globulin levels have remained unaltered after intravenous injection of this polysaccharide. Hepatic catheterization in a few patients has indicated a questionably increased hepatic blood flow, no significant evidence of dextran removal by the liver, and no alterations in hepatic glucose metabolism.

Plasma volume expansion has been studied by hematocrit, plasma protein, and dye techniques. All three methods have indicated a 10 to 15% increase in plasma volume after injection of 500 cc. of dextran and a 15 to 20% increase after 1,000 cc. of dextran has been given.

Our studies have shown that the mean plasma level of dextran is 726 mg. per 100 cc. ± 29 standard error after the injection of 500 cc. of 6% dextran. The level slowly falls and at 96 hours after injection is 88 mg. ± 5. Most of the urine dextran excretion occurs in the first 48 hours and accounts for 42% of the injected material. The fate of the remaining material is being investigated. Electrophoretic studies of dextran in the plasma of patients indicates that the polysaccharide does

not migrate at pH 8.4 but appears in the boundary anomaly. The dextran peak can be observed for 72 hours (approximately 100 mg. of dextran concentration per 100 cc.). No alterations in the electrophoretic characteristics of the serum proteins were observed.

The group of patients studied in this investigation had a number of different diagnoses, given in the following table.

Diseases in Which Dextran Has Been Injected

Category	Number of Patients
Infection	15
Cardiovascular disease	10
Gastrointestinal disease	6
Neurological disease	3
Anxiety	5
Neoplasia	2
Arthritis	3
Miscellaneous	6

No reactions have been observed in this study, but it must be remembered that only American dextran has been used.

In summary, it might be added that no untoward reactions or functional impairment of the hematopoietic, circulatory, renal or hepatic systems has been observed. Dextran effectively produces and maintains hemodilution and has the desired qualities of a plasma volume expander. The conclusions have been substantiated in 52 patients in shock as a result of blood loss and trauma. Forty-four of these patients responded to dextran administration, five patients had a temporary response, and three patients had no response. Clinical laboratory studies have shown plasma volume expansion and increased cardiac output and urine output in these patients.

Expandex was kindly supplied by Commercial Solvents Corporation.

PRESENT STATUS OF PLASMA VOLUME EXPANDERS IN THE TREATMENT OF SHOCK

Clinical Results in Surgery

WINCHELL McK. CRAIG, M.D.
HOWARD K. GRAY, M.D.
AND
JOHN S. LUNDY, M.D.
ROCHESTER, MINN.

OPERATIONS on the sympathetic nervous system for the relief of progressive hypertension have been followed by interesting reactions. A decided decrease in blood pressure is the object of the operation. However, it was early noticed that a too sudden and prolonged decrease in blood pressure had the effect of shock on the patients. This occurred during and after the operation. The subjective effect was that of prostration and weakness to the extent that these two factors interfered with convalescence, and the second-stage procedure, which usually is done a week or 10 days after the first, was delayed. Blood was transfused during and after the operation, and the patient's condition was improved. It seemed to us that the intravenous administration of plasma or a plasma substitute would give the necessary support of blood volume that the transfusion of blood had given, inasmuch as there was little loss of blood during this particular operation.

Solution of dextran was used early in 1946. We were gratified to note that the blood pressure was sustained during the interval between stages of the operation. The patient was subjectively much improved and after the first-stage procedure could be out of bed on the third postoperative day. The second stage of the operation could be done as early as the fifth postoperative day. It was observed that after the second stage there was not the usual decrease in blood pressure, causing prostration of the patient. Again, he could be up on the third postoperative day.

By the use of solution of dextran the immediate postoperative decrease in blood pressure was much less and not so incapacitating, the interval between stages of the operation was shortened, and the hospital stay of the patient was markedly reduced. Periston also was tried. It proved almost as efficacious. By the use of such agents the shock-like decrease in blood pressure immediately after the operation has been eliminated, because blood volume has been maintained during the acute vasodilation which follows section of the thoracolumbar sympathetic system.

From the Section of Neurologic Surgery (Dr. Craig), the Division of Surgery (Dr. Gray) and the Section of Anesthesiology (Dr. Lundy), Mayo Clinic.

Read before the Section on Anesthesiology as part of a symposium on Plasma Volume Expanders in the Treatment of Shock at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

Three and a half per cent polyvinylpyrrolidone in Ringer's solution (periston or P. V. P. solution) has been used in about 200 instances, and gelatin (plasmoid) has been used in a series of more than 500 cases. Occasionally it was found desirable to administer a vasopressor agent in conjunction with the plasma volume expanders, but usually that was not necessary when solutions of dextran or periston were used. Sometimes it was necessary when gelatin was employed.

Treatment of a patient with a plasma volume expander for shock, plus the use of blood, could be called "balanced supportive therapy." Usually better results are obtained when both are used than when either one is used alone.[1]

RATIONALE OF USE OF PLASMA VOLUME EXPANDERS

During anesthesia and operation there are occasions on which the blood pressure does not remain at a satisfactory level. Since April, 1946, a 6% solution of dextran in isotonic solution of sodium chloride has been used in about 2,000 instances to produce and maintain blood pressure at a satisfactory value. No effort has been made to avoid the use of blood, however, because it has not been considered that these new materials, commonly called "blood substitutes," can take the place of blood except when only a little blood has been lost. We wish to emphasize the point that if a patient needs blood, he should have it. Blood has been administered together with the new materials under consideration whenever it was felt that such a measure was indicated by the patient's poor response to transfusions.

In a series of 50 unanesthetized patients who were recovering from operations that had been done several days previously we were able to administer 100 to 250 cc. of solution of dextran intravenously. Both the Swedish product, "macrodex," and the English product, "intradex," were used. Reaction occurred in only one patient. The contents of one bottle were divided into two portions of 250 cc. each.

The first 250 cc. was administered to the first unanesthetized patient without untoward reaction. As soon as 50 cc. of the material had been administered to the second patient, however, he sat bolt upright in bed, a projectile type of vomiting developed, and he fell back into a condition resembling a faint. He was treated by the intravenous injection of ephedrine and recovered within a short time.

The foregoing experience led us to inquire of Dr. D. R. Mathieson whether or not skin testing patients for sensitivity to dextran would be worth while; this testing procedure is now being undertaken. Sensitivity to dextran might be found, for Hehre and Sugg [2] have reported that sensitivity to this agent can be produced in guinea pigs. Pulaski has demonstrated to one of us (Lundy) intolerance on the part of unanesthetized patients to Swedish dextran and British dextran but not to the dextran made in this country.

Although the immediate mortality rate after thoracolumbar sympathetic ganglionectomy and splanchnic resection has been very low, we have had several instances in which patients died of acute coronary occlusion five to 10 days after the second-stage operation. At necropsy there were no discernible ill effects attributable to dextran. The kidneys were examined both grossly and microscopically.

1. Lundy, J. S.: Balanced Supportive Therapy During Anesthesia, Northwest Med. 50:341-343 (May) 1951.

2. Hehre, E. J., and Sugg, J. Y.: Serological Reactivity of Dextran Plasma Substitute, Federation Proc. 9:383 (March) 1950.

It seems clear that plasma volume expanders are a considerable addition to measures that have been available previously; clinically, it is easily demonstrated that blood pressure can be elevated by them.

Clinically, also, one is guided by the general appearance of the patient, blood pressure and pulse. Shock, as the word is used in this paper, is a state in which the patient is pale, with a cool and moist skin, in contrast to the person not in shock, who is pink, with a warm and dry skin. The blood pressure of the patient in shock is low, as is the pulse pressure. In the patient who has been treated for shock with satisfactory results the blood pressure is elevated to at least 100 mm. of mercury systolic and the pulse pressure is sufficient for it to be described, on palpation, as a "good" pulse. We have seen no untoward reactions result from the use of plasma volume expanders in anesthetized patients.

REPORT OF TWO ILLUSTRATIVE CASES

CASE 1.—The preoperative diagnosis was perforating carcinoma of the splenic flexure of the colon, involving the greater curvature of the stomach. On March 10, 1950, 500 cc. of blood was given in transfusion to the patient because of anemia. The patient was operated on on March 13, 1950, and during the operation he received 1,000 cc. of blood. The operation was resection of a portion of the transverse colon, splenic flexure and a portion of the descending colon, with performance of partial gastrectomy, splenectomy, partial pancreatectomy and greater omentectomy (exteriorization of the ends of the transverse and descending portions of the colon, clamp method). The operation and anesthesia lasted two hours and thirty-five minutes. The anesthesia was induced with nitrous oxide and oxygen and ether and was maintained with ether. An intratracheal tube was used for an airway. The administration of anesthetic agents was stopped a good half-hour before the operation was over, but the patient showed no signs of recovering consciousness. When the operation was finished, it was felt that the patient should be taken to the anesthesia room, where he was kept for an additional hour. During that period he received two bottles (380 cc. each) of a solution of what was then called "dextran pH," prepared in Sweden, but he still showed very little improvement. His son was a physician; he stayed with us while we treated him. When about half of the third bottle of solution of dextran, containing 380 cc., had been administered, the patient's pulse improved, blood pressure increased and pulse pressure increased, and by the time we had finished the administration of the third bottle the patient opened his eyes when asked to do so.

CASE 2.—The operation was resection of a portion of the ileum and cecum and a portion of the ascending colon; ileocolostomy and closure of an opening in the upper part of the ileum also were performed. The diagnosis was multiple ileocutaneous fistulas. The patient, a woman, received 500 cc. of blood on Sept. 23, 1949. She was operated on on September 29. During the operation she received 3,850 cc. of blood. After operation she received 4,750 cc. of blood and 1,000 cc. of a 5% solution of dextrose and was placed in an oxygen tent. The next day she received 2,500 cc. of blood. She appeared to be dying. She was given 760 cc. of a 6% solution of dextran pH; the blood pressure increased to 100 mm. of mercury systolic, and the pulse rate became satisfactory. She was removed from the oxygen tent and made a satisfactory recovery.

COMMENT

It is our opinion that, generally speaking, when materials such as dextran, periston and gelatin are indicated they might be used prophylactically in the treatment of shock by starting the administration of one of them as soon as surgical exploration has been completed and the decision is made to do a major operation. We believe that as the operations take on more and more the characteristics of major procedures, the use of blood and of one of the plasma volume expanders is at present the most satisfactory way of maintaining a circulating volume in the cardiovascular system, which is the essential treatment of surgical shock.

ABSTRACT OF DISCUSSION

DR. I. S. RAVDIN, Philadelphia: You have heard a group of papers presented in this section today which are important from the standpoint of not only civilian surgery but also the nation in the event of any future catastrophe. Under the conditions of modern warfare, it is highly likely that we shall not have the amount of blood adequately necessary to take care of the casualties which may occur. It is for this reason, as you have perhaps felt this morning, that efforts are being made to find those agents which will correct a deficiency of an effective plasma volume.

The agents which have been spoken about today are agents which exert their effects through their colloidal osmotic pressure. Time will not permit me to discuss each of these papers separately, but I should like to make these few remarks in general about the subject.

There is no substitute for blood. This was adequately demonstrated during the last war by medical officers who took care of many casualties. When there was a sufficient amount of blood, they used blood in the field to the extent of four to six times as much as they used plasma. However, blood can be kept only for a period of three weeks. Efforts are being made to extend the life of the red cell. Both blood and plasma at this time have the great danger of transmitting viruses, and we do not have a proved test as yet which has demonstrated without any challenge the effectiveness of methods now being used to sterilize even plasma.

We have studied gelatin for 13 years. Its defect from the standpoint of use by the military is the fact that it jells. Regardless of what Dr. Hartman said this morning, osseous gelatin has no effect on renal function. We have administered gelatin to a dog for as long as 112 days continually. Seven days after cessation of the injections, histologic studies showed a completely normal kidney. Studies made in man by Dr. Mitchie of my department, after the injection of as much as 1,000 to 2,000 cc. of gelatin per day for eight days, showed no change in glomerular or tubular function.

When we speak of dextran, we must remember that we are speaking of a variety of substances. There is not one dextran. There are many dextrans, and each manufacturer now making such a material has a different material. All these agents are macromolecular substances; none of them now available, except for the most limited type of experimental scrutiny, are substances within even a small area of molecular size. Swedish dextran undoubtedly varies in molecular size from around 20,000 to perhaps over 200,000. I call your attention to the fact that although certain of these papers today have indicated that the substances has specific molecular ranges, such material has not been available for clinical use. Dextran is an effective volume expander, either in the dog or in man. We have studied it in man from the standpoint of hemodynamics, from the standpoint of renal function, and from the standpoint of hepatic function.

I call your attention to the fact that as far as gelatin (and, I am sure, dextran) is concerned, some of the changes shown in the slides of Dr. Hartman are represented by the fact that there is gelatin in the tubules. These are not casts; this is secreted gelatin, and it can be demonstrated by proper studies.

PVP, or polyvinylpyrrolidone, represents, again, a variety of substances, made by different manufacturers, and it is of varying molecular size. We have studied this material and so far have found no effect on renal, hepatic or dynamic functions of the circulation.

We have recently been conducting limited experiments in dogs with polyglucose.

The important thing is that we shall not have a "red herring" pulled into this meeting which will impede progress necessary for our national safety by a belief that these histologic changes indicate clearly that there is an impairment of function of an organ. We have done all the functional studies in man now available to investigators with these agents, and, with the exception of some very minor temporary changes in an occasional patient in hepatic function, they are clinically safe in man. They are plasma volume expanders, and they are extenders in that they will increase the opportunity for usefulness of human plasma.

DR. EDWIN J. PULASKI, San Antonio, Texas: The papers just presented give important and convincing evidence that dextran is a useful and effective plasma volume expander, and our own studies are in full agreement. One factor which bears on the utility of dextran as safe blood plasma substitute is its fate in the body after infusion. One of our studies has concerned itself with attempts to determine what happens to the dextran which is unaccounted for by excretion in urine. Like Bloom, we could not measure important amounts in bile or in the gastrointestinal tract of dogs. The next experiments concerned the possible metabolism of dextran. In our laboratories, Gray, using the starved, phlorhizinized dog as a medium for these experiments,

observed an increase in excretion of dextrose during the 24 to 48-hour period following intravenous administration of dextran. This could only be explained on the basis that some of the dextran which is unexcreted is metabolized to glucose. If this conclusion is valid, there should be less concern over possible harmful effects of dextran due to prolonged storage in body tissues.

Our studies on dextran in "normal," unanesthetized human volunteers (soldiers) suggest variations in the types now available. Dextran of foreign manufacture caused reactions not unlike those of serum sickness in 40% of 100 soldiers. These reactions varied from urticaria to respiratory distress and fall in blood pressure, which occurred 5 to 45 minutes after the infusion was started, often followed by limb edema after subsidence of the acute episode. Prior administration of morphine, antihistaminics, cortisone or adrenal cortical hormone did not influence the incidence or severity of these reactions. In anesthetized subjects and in patients in shock, urticaria only was observed, the incidence being 6%. With dextran of American manufacture, only one reaction, urticaria, occurred in 100 unanesthetized volunteers. Two volunteers who reacted after infusion of foreign-made dextran did not react five days later to American-made material; two volunteers who reacted to foreign-made dextran reacted once again to infusion of another batch of foreign-made material. We are unable to account for the high incidence of reactions in unanesthetized soldiers with dextran of foreign manufacture, which is in contrast to a low rate of reactivity reported from civilian hospitals here and abroad.

DR. DONALD E. HALE, Cleveland: The papers presented this morning have indicated the value of the various plasma volume expanders and have pointed out the possible dangers. We are reminded that no agent used in our specialty is free from danger if used unwisely or in excess.

Findings of careful workers are somewhat at variance. Although microscopic changes are found in certain organs, function does not seem to be disturbed. Clinical experience seems to find small fault with certain of the macromolecular substances.

Opinions differ as to the advisability of using a plasma volume expander to replace moderate blood loss. Those surgeons who regard transfusion as a barely sublethal procedure at best find the expanders of especially high merit. Some believe that in a patient of normal blood volume and hemoglobin undergoing uncomplicated surgery a blood loss of 500 to 1,000 cc. may be made up at the time with an equal quantity of expander. A larger blood loss should be an indication for whole blood transfusion.

According to Kolff, dextran is an especially valuable colloid for treatment of hypotensive states in the presence of uremia or anuria. This is one case in which a substitute is better than blood. If such a patient is treated with blood or plasma, the catabolites of these substances cause a further rise in blood urea. Dextran, on the other hand, may be broken down, at least partially, into glucose, which is gratefully metabolized by the starving patient.

Macromolecular substances may be used for expanding plasma at the expense of body fluids. We have used dextran 20% a few times in an effort to reduce brain edema.

It has been mentioned that dextran has been used in different molecular weights and in different concentrations. It would be of interest to have specific recommendations as to the optimum molecular weight and concentration for its ordinary use as a plasma volume expander. Solutions prepared in distilled water or glucose solution might be preferable for use in patients to whom excess sodium chloride must not be given. Even a 20% dextran, if in sterile distilled water only, will cause hemolysis of the red cells, and on this account it must be given in either saline or 5% dextrose solution.

A plasma expander, to be of optimal value, must be given as the need arises, or as soon thereafter as possible. Clear indications for its use are obvious blood loss, falling blood pressure and rising pulse. One should not wait for signs of frank shock. Knowledge of preoperative hemoglobin and blood volume levels and some method of measuring operative blood loss help in directing a logical replacement program. Means of infusion—by vein, marrow, or artery—should be adequate and available in anticipation of the need.

DR. LLOYD R. NEWHOUSER, United States Naval Hospital, Chelsea, Mass.: I think we have heard ample evidence this morning that gelatin, dextran and PVP are effective in restoring and maintaining the blood volume in human beings as well as in experimental animals.

Dr. Bollman pointed out that the 24,000 molecular-size dextran was no more effective than saline. That brings up the point of what should be the ideal size or weight, as Dr. Hale mentioned. Serum albumin is approximately 65,000 molecular size, and this may be approximately the ideal size. However, the firms producing dextran have to abide by extremely rigid

specifications if we are to have a satisfactory volume expander with dextran. We do not want material that ranges from 20,000 up to, say, 400,000. It should be much more confined, maybe 40,000 or 50,000 to 80,000, and we do not want a great deal of it at a high molecular size.

Dr. Bloom's studies indicate that the 6% dextran results from his attempt to get a 5% serum albumin solution.

Dr. Hartman gave us a warning on the indiscriminate use of this material. I wonder if he found any more pathologic changes than we would find after using human plasma with a mercurial added, as we did during the major portion of the last war. I think we all agree that that is not good procedure today.

Dr. Craig mentioned that plasma substitutes cannot take the place of blood. Dr. Ravdin mentioned that, too. I should like to emphasize again that there is no substitute for whole blood; we consider the use of plasma, serum, and albumin as only a first-aid measure, as we did during the last war. We should consider gelatin, dextran, and polyvinylpyrrolidone as merely first-aid measures if we use them for the treatment of shock.

Dr. Bloom stated that we have no difficulty in blood grouping, cross mixing with Rh typing. This is true with certain dextrans, but it is my impression that it is not true when you have dextran with a very high molecular size. In Dr. Bloom's case the blood level was high enough for him to encounter difficulty.

We must be on guard constantly when we are using any of these preparations. You may find times when you do encounter some difficulty; as was brought out, there is evidence that there is only one satisfactory dextran produced in this country. However, we hope that within a comparatively short time there will be others. By "satisfactory" I mean materials which restore and maintain plasma volume that are hygienic, nonantigenic, nontoxic and nonpyrogenic. As Colonel Pulaski brought out, perhaps not all of this material is nonantigenic.

At the present time it is gratifying to know we have these additional plasma expanders available not only in the armed services but in civilian medicine as well. While there is not a large supply of these materials at the present time, they will become available in the near future, and, as Dr. Ravdin brought out, we should take steps to have them in reserve.

I should like to say that we still need a large and efficient national blood program, in spite of all this. Unless such a program is in operation at a time when disaster might strike this country, it would be far too late.

DR. DOUGLAS B. KENDRICK, JR., Washington, D. C.: These excellent papers have been discussed adequately, and I can add little more to the discussion, but I should like to state before this group the stand that the armed forces have taken with regard to plasma substitutes.

We have been interested in substitutes for plasma in blood since World War I. During the second world war, in 1943, we had made available to us some captive supplies that the Germans had been using. There was only limited interest in the material at that time, because we were so busy working on the whole blood program. During World War II we were exceedingly fortunate in having contributions of blood to such an extent that we were able to supply all our needs for the armed forces.

At the present time we are again engaged in a similar program, trying to stockpile adequate quantities of plasma and, at the same time, to furnish whole blood for use in Korea. Obviously, with the increased need of the civilian defense program, in addition to that of the armed forces, we must consider other sources of supply for plasma expanders. We realize we can get a certain quantity of plasma, and it will do an adequate job for us, but at the same time we must supplement the requirements of the armed forces and civilian defense with expanders such as have been discussed today.

With the idea in mind of trying to determine the best expanders to procure, we have leaned heavily on the National Research Council and the chemical groups that have been working on periston, dextran and other expanders. Today, on the bases of the papers you have heard here and also from the work that has been done by the National Research Council, it appears that the best expander at the present time is dextran. With that in mind, we have developed specifications for a dextran which will provide a nontoxic, nonpyrogenic, nonantigenic substance, if we can obtain such, and a molecular size or range of approximately 80,000 plus or minus 25,000. Let us say that none of this material should go below 25,000, and, if possible, none should go above 200,000. I think some of the Swedish dextrans have gone up as high as 270,000. With this in mind, we have prepared these specifications, and they are now being used for contracting with an

American source of supply to provide limited quantities of dextran for the use of the armed services.

By making these preliminary educational contracts, we hope that other firms will begin to develop their capabilities of production and, in turn, will have their products approved by the National Research Council. In order to meet the specifications, we are carrying out the necessary laboratory and clinical tests on all samples produced, and it is hoped that in this way we may have a running account of acceptability of material that is manufactured for us.

Again, we should like to say that the program for expanders is a supplemental one and that there is nothing to take the place of whole blood, as has been demonstrated in Korea many, many times. However, in addition to whole blood, we must have plasma and expanders of this type. We are very glad to have the information that has been supplied to us today. It will be used accordingly.

DR. FREDERICK M. ALLEN, New York: The plasma superstition, which was originated and then perpetuated by the Shock Committees of the first and second world wars, is the doctrine that the blood volume in shock depends on water binding by colloids and that salt solution is both useless and harmful because it passes quickly out of the vessels and carries some of the precious plasma proteins with it. Only after long experiments and with some trepidation I became the first to contradict this universally accepted falsehood, which was standard in all textbooks. After my publication in 1939 the experimental reports became reversed, and not a single investigator has since claimed that saline is useless or harmful. Clinical confirmations ensued. After the German surrender the same authorities who had ignored my work and imposed rigid plasma treatment (undoubtedly at the cost of many lives) published a recommendation (*The Journal of the American Medical Association* **128**:475-479 [June 16] 1945) for treating shock chiefly with large volumes of saline plus a small fraction of plasma. Others confirm the fact that saline saves as many shocked animals as plasma (Harkins, Rosenthal, Prinzmetal, and others). Dialyzed plasma and other colloids are valueless (Winternitz). The use of dextran at least adds agreement that the nutritive need for plasma is imaginary. Dextran lacks the only therapeutic proofs, namely, that in saline solution it saves more lives than saline alone or that it has any value without salt. The emphasis on merely supplying fluid or expanding plasma volume is fallacious. I agree that rats and mice furnish no decisive clinical guidance, but dogs are surgically reliable, and, recalling the quarter century of positive and unanimous agreement of surgeons on the worthlessness of saline, I still distrust empiric clinical impressions which contravene precise dog experiments.

The scientific proof is clear that sodium salt solution specifically combats the vascular atony of shock, and colloids have nothing whatever to do with it. This is, of course, the obverse of the specific reduction of hypertension by withdrawal of salt, which the academic authorities likewise attacked. In hemorrhage, salt solution has no such specificity as in shock; nevertheless its value is much greater than generally recognized, as pointed out in my recent paper (*Journal of the International College of Surgeons* **15**:201-211, 1951), which adds references also on shock. In an atomic bombing emergency, the lingering superstition may cost lives by causing delay to await supplies of plasma or colloid substitutes, whereas instructions should emphasize the vital necessity of the promptest possible treatment with material abundantly at hand, namely, salt solution.

DR. JOHN SCUDDER, New York: I should like to add a word of caution. We tested dextran in 1946 and gave it up because of severe anaphylactic shock occurring in some unpredictable cases. This was at variance with the Mayo Clinic's findings. We were a little perturbed as to why they in Rochester got one effect and we in New York got another.

In 1949 we tested a second batch of dextran prepared by Pharmacia and sent to us from Sweden, so that there would be no mistake in the type we were using. After giving 2 cc. to one of our medical students recovering from an appendicitis operation, we had to give artificial respiration and ephedrine to bring him back to life. This rather disturbed us, and we gave up the use of dextran.

I think the answer possibly lies in the fact that in New York City we may be heavily contaminated (and we are trying to prove it) with the pneumococci, Types II, XII, and XX. The polysaccharides of these pneumococci cross react with dextran, and so possibly some of these severe reactions may have been due to the fact that the patients previously had pneumonia due to one of these pneumococci.

We took the problem to Dr. Michael Heidelberger, who has prepared for us solutions of these three polysaccharides. Mr. Bryan of our medical school is testing out students, nurses and others in sufficient numbers to find out whether the cross reaction with pneumococci, Types II, XII, and XX, is the explanation for some of these reactions and the reason why our report differs from others.

We use the skin test on either arm, employing these polysaccharides, dextran, and phenol-saline control.

General George E. Armstrong asked me if I would order a million units of dextran if I were he. I said: "Yes, because there is no doubt that dextran is a very effective plasma volume extender." You can bleed a dog until the hematocrit level is down to 9% and the animal will appear to be dead, but if you give a transfusion of dextran solution immediately, the dog gets up and walks around the room. When you do that a sufficient number of times, you realize that there is something which this plasma volume extender can do that saline cannot do.

DR. JESSE L. BOLLMAN, Rochester, Minn.: I should like to recount an experience which emphasizes the point that Dr. Ravdin made about the apparently unnecessary worry regarding the deposition of these substances in the tissue. It also bears on Dr. Hale's point in mentioning the fact that we are always dealing with poisons. Colloids are poisons if given in excess, and it is necessary to bear in mind the relation between the effective dose and the dose that is too much.

A number of years ago, when we were still interested in acacia, we injected large amounts of it into dogs, and edema and ascites developed, because we gave them too much. We gave them as much as possible and repeated injections every week or so for six months, and by that time their livers contained large amounts of acacia. Two of the animals lived for about 10 years, their livers still containing large amounts of acacia; however, functional tests did not show any impairment of the liver. There were no ascites except of a temporary nature from overtreatment, and the animals lived uneventful lives for 10 years, a fairly long life for a dog in our laboratories. Liver biopsies at intervals during this time revealed the presence of acacia which did not produce any reaction in the liver.

DR. WALTER L. BLOOM, Emory University, Ga.: I wish to thank the various discussers for their comments. They have raised as many problems in their discussions as we have raised in our presentation of data.

If we can eventually show that dextran is metabolized, in keeping with the data discussed by Colonel Pulaski and with the data of other investigations now under way on this subject, then dextran's value therapeutically becomes much greater. If this substance is metabolized, we are approaching the goal that we have set for ourselves in this problem, which is the finding of an adequate plasma volume expander which will eventually be completely excreted or metabolized.

Dr. Ravdin's point that these materials are not homogeneous must be heeded. The materials are mixtures not only with respect to molecular weight but also with respect to molecular shape and structure. These are the factors we are eventually going to understand and control. The urgency of the problem indicates that these studies will have to be carried out along with our clinical studies rather than antedating them.

The reactions which Colonel Pulaski has observed following dextran injection constitute a most interesting phenomena since some dextran preparations do not cause the reaction. The mechanism of this reaction is unknown and must be answered before we are completely satisfied with this plasma volume expander.

Captain Newhouser's suggestion about studying the effects of loading the organism with a substance such as albumin must be used as control in all such experiments on plasma volume expanders.

A statement with respect to the use of saline in shock is going to involve me in the polemics of a rather heated discussion. It might be emphasized that no doubt exists concerning the findings of Rosenthal and his group. Their studies present excellent data on experimental therapy in the mouse, but as far as man is concerned the observation has not been adequately confirmed. The problem that arises in this discussion deals with where and when saline should be used and not with whether it should be used. In the presence of my peers at this meeting, who have worked a long time with problems of shock and who are not satisfied with saline alone in its treatment, I find conviction that we still need a substance to expand and maintain plasma volume.

DR. WINCHELL MCK. CRAIG, Rochester, Minn.: In concluding this most interesting and, I think, inspiring discussion, I can only say how much we all appreciate the discussion that has been given.

SUBCOSTOSTERNAL (MORGAGNI) DIAPHRAGMATIC HERNIA

Report of a Case of Hernia Containing Stomach, Transverse Colon, and Omentum, with Review of the Literature

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DETROIT

DIAPHRAGMATIC hernias may be divided (after Harrington) into two groups: (1) traumatic (including inflammatory necrosis) and (2) non-traumatic. The latter are structural deficiencies, which may be congenital or acquired. They include (1) esophageal hiatus hernia, due to deficiency of the circular muscle bundles of the hiatus; (2) hernia through the foramen of Bochdalek (pleuroperitoneal hiatus), in which the posterolateral portion of the diaphragm, usually on the left side, fails to fuse; (3) congenital absence of the diaphragm—an enlargement of the foregoing—virtually a more extensive congenital defect extending farther posteriorly, and (4) herniation anteriorly through the foramen of Morgagni or Larrey's spaces. These are the two small spaces devoid of muscle, situated anteriorly on either side of the sternum and immediately behind the anterior costal attachment of the diaphragm. They are filled with loose areolar tissues and contain only the superior epigastric artery and lymphatics. Such a hernia has also been called retrosternal, parasternal, or anterior diaphragmatic hernia. Harrington suggests the term subcostosternal diaphragmatic hernia, since it may occur on either side of the midline. Such malformations are rare. There is always a sac present, as in hiatus hernia (the other congenital hernias do not have a sac). The round ligament is in close association with the sac.

We wish to report an instance of this type of hernia, which contained the stomach, transverse colon and omentum in the right thoracic cavity. There was severe alkalosis and hypokalemia due to the pyloric obstruction. Also, we have briefly reviewed the case reports and incidence of this lesion as found in the literature.

INCIDENCE

Roughly, in several series of cases of diaphragmatic hernia, the incidence of subcostosternal hernia is 2.6% (Table 1).[1]

From the Surgical Service of Harper Hospital.

1. Donovan, E. J.: Congenital Diaphragmatic Hernia, Ann. Surg. **122**:569-581 (Oct.) 1945. Strayer, J. W.: Diaphragmatic Hernia, J. Michigan M. Soc. **48**:1254-1263 (Oct.) 1949. Harper Hospital, Case #329792; Case #A-58917 (Dr. Saltzstein). Harrington, S. W.: Subcostosternal Diaphragmatic Hernias (Foramen of Morgagni), Surg., Gynec. & Obst. **73**:601-614 (Nov.) 1941; Surgical Treatment of the More Common Types of Diaphragmatic Hernia, Ann. Surg. **122**:546-568 (Oct.) 1945. Adams, R., and Lee, W. F., Jr.: Diaphragmatic Hernia: Clinical Report of 34 Surgically Treated Cases, S. Clin. North America **26**:742-750 (June) 1946. Stobie, G. H.: Diaphragmatic Hernia, Canad. M. A. J. **36**:136-141 (Feb.) 1937.

We have collected 44 cases of subcostosternal hernias from the literature. The case we herewith report makes 45. In 21 the diagnosis was proved by operation, in 7 by autopsy, and in 17 by x-ray only. We have included the last cases provided we felt reasonably certain that the diagnosis was positive.

SEX DIFFERENCES

There were 22 male and 23 female patients (Table 2). From infancy to 12 years, sex incidence was equal. Males predominate in early adult life to age 40, but in the older age group (age 50 and above), there are approximately two and one-half times as many females as males.

TABLE 1.—*Incidence of Different Types of Diaphragmatic Hernia*

Author and Date	Total No. of Cases	Esophageal	Bochdalek	Congenital Absence	Subcosto-sternal (Morgagni)	Other
Donovan, 1945	17	1	9	1	2	4
Strayer, 1949	158	131	7	..	3	17
Harrington, 1948	430	343	9	12	8	58 (traumatic)
Adams and Lee, 1946	34	22	5	..	3	4
Stobie, 1937	5	..	..	..	1	4
Harper Hospital, 1938-1949	36	32	..	1	1	2
Total	680	529	30	14	18	89
%	...	77.8	4.4	2.0	2.6	13.1

TABLE 2.—*Age and Sex Incidence of Subcostosternal Diaphragmatic Hernia*

Age Group	Male	Female
0-12	4	4
13-29	6	0
30-39	5	1
40-49	1	2
50-59	0	7
60-69	3	4
70-79	2	5
80-89	1	0
Total	22	23

SYMPTOMATOLOGY AS RELATED TO CONTENTS OF SAC

An attempt was made to correlate the contents of the sac with age groups (Table 3) and with the symptomatology (Table 4).[2]

2. Althabe, A.; di Paola, G., and Flachsland Siburu, E.: Subcostosternal Diaphragmatic Hernia: Case, Semana méd. **1**:17-22 (Jan. 6) 1944. Bell, J. C., and Heublein, G. W.: Diagnostic Roentgenology in an Army General Hospital During the Present War, Radiology **43**:425-485 (Nov.) 1944. Büttner, A.: Parasternal Hernia and Lipoma of Diaphragm, Arch. klin. Chir. **202**:154-170 (Sept.) 1941. Camerer, J. W.: Right-Sided Parasternal Hernia of Liver: Case, Fortschr. Geb. Röntgenstrahlen **62**:262-265 (Oct.) 1940. Cassinelli, J., and Tiscornia, R. E.: Right Anterior Congenital Diaphragmatic Hernia in Infants (Hernia of the Hiatus of Morgagni, Harrington's Subcostosternal Hernia), Arch. pediat. Uruguay **18**:296-312 (July); 376-391 (Aug.) 1947. Caumartin, H. T.: Roentgenological and Clinical Studies in 8 cases of Unusual Gastrointestinal Diseases, Grace Hosp. Bull. **26**(No. 2):101-119 (July) 1948. Colmers, R. A.: Parasternal Diaphragmatic Hernia with Report of a Case on Right Side: (Accompanied by Acquired Atelectasis), Radiology **37**:733-739 (Dec.) 1941. Curri, D.: A

(Footnote continued on next page)

GROUP 1

The 45 cases fall into two large groups. Group 1 comprises eight cases. The patients ranged from infancy to 12 years. Of these, four were Mongolian idiots, two were feebleminded, and one showed multiple congenital deformities Table 4.*A*).

The contents of the hernia sac were liver only in two cases of this group; colon only in one case; colon and liver in one case, and small bowel only in one case. No hernia sacs contained stomach or omentum. Symptoms in this group were primarily chest symptoms: suffocation, cyanosis, dyspnea, and cough. When abdominal symptoms occurred, they were chiefly what one might expect in young children, i. e., vomiting, diarrhea, anorexia, and feeding problems. In only one child did partial intestinal obstruction occur; this was the patient whose hernia sac contained small bowel.

GROUP 2

Group 2, the larger group, comprises the remainder of the cases. There were no descriptions of concomitant gross congenital abnormalities in this group. As seen from Table 3, there are only four patients from 13 to 29 years of age. Three of these were reported from an induction center in the routine examination of 4,000 chests

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Case of Non-Incarcerated, True, Parasternal Right-Sided Diaphragmatic Hernia, Beitr. klin. Chir. **149**:446-456, 1930. Eerland, L. D.: True Parasternal Diaphragmatic Hernia at the Right, Simulating Terato-Dermoid of Anterior Mediastinum: Case, Nederl. tijdschr. geneesk. **90**:1450-1452 (Oct. 19) 1946. Ellinger, E.: Rare Form (Parasternal Hernia), Röntgenpraxis **11**:490-502 (Aug.) 1939. Funck-Brentano, P.; Megnin, J., and Allard, P.: Medio-Sternal Diaphragmatic Hernia, Ann. anat. path. **10**:401-405 (April) 1933. von Greyerz, W.: Hernia Diaphragmatica Retrosternalis, Acta radiol. **18**:428-438, 1937. Hodges, F. J.: The Gastro-intestinal Tract, a Handbook of Roentgen Diagnosis, Chicago, The Year Book Publishers, Inc., 1944, pp. 266-267. Jamain and Saks: Gigantic Congenital Retrosternal Diaphragmatic Hernia, Ann. anat. path. **16**:1224-1228, 1940. Kaiser, R.: Right-Sided Parasternal Hernia of the Stomach, Röntgenpraxis **12**:180-182 (May) 1940. Kernau, T.: Rare Case of Bilateral Parasternal Diaphragmatic Hernia, ibid. **12**:28-30 (Jan.) 1940. Kratzeisen, E.: Retrosternal Diaphragmatic Hernia, Arch. path. Anat. **232**:227-231, 1921. Lambranzi, M.: Right Parasternal Diaphragmatic Hernia: Case, Quaderni radiol. **3**:125-129, 1932. Landivar, A. F.; Brea, M. M. J.; Santas, A. A., and Martinez, J. L.: Subcostosternal Diaphragmatic Hernia: Study Apropos of 3 Cases, Bol. y trab. Acad. argent. cir. **31**:984-997 (Nov. 12) 1947. Leszler, A.: Right-Sided Diaphragmatic Hernia Complicated by Gastric Obstruction, Röntgenpraxis **13**:267-269 (July) 1941. May, E. A.: Bilateral Diaphragmatic Hernia, Radiology **20**:275-281 (April) 1933. Meade, R. H., and Ravdin, I. S.: Non-Traumatic Hernia Through Right Parasternal Foramen of Morgagni, Ann. Surg. **102**:465-471 (Sept.) 1935. Parrella, G. S., and Hurwitz, A.: Repair of Anterior Subcostosternal Hernia of the Diaphragm (Hernia of Morgagni) Using a Flap of Transversalis Fascia, Arch. Surg. **59**:1327-1334 (Dec.) 1949. Polák, E., and Sváb, V.: An Unusual Operative Approach in a Case of Left-Sided Retrosternal Diaphragmatic Hernia, J. Internat. Coll. Surgeons **10**:549-552 (Sept.-Oct.) 1947. Reich, L.: A Collection of Illustrative Cases of Diaphragmatic Hernia, Fortschr. Geb. Röntgenstrahlen **30**:305-319, 1923; Right-Sided Parasternal Diaphragmatic Hernia, Mitt. Gesellsch. inn. Med. u. Kinderh. **21**:27-30, 1922. Rocha, A.: Right Diaphragmatic Hernia Simulating a Pulmonary Cyst, Med. clín. **3**:498-502 (Dec.) 1944. Sielmann, H.: A Case of Parasternal Diaphragmatic Hernia at the Right, Fortschr. Geb. Röntgenstrahle **32**:426-430, 1924. Signorini, J. P. A.: Diaphragmatic Hernias, Rev. méd.-quir. pat. fem. **21**:227-247 (April) 1943. Steuer, K.: Right Parasternal Diaphragmatic Hernia: Case, Röntgenpraxis **9**:788-792 (Nov.) 1937. Thorell, E.: Case of Diaphragmatic Hernia in Larrey's Space (Trigonum Sternocostale), Nord. med. **28**:2561-2563 (Dec. 7) 1945. Valledor, T., and Gomez Tejera, D.: Right Diaphragmatic Hernia of Colon Through Hiatus of Morgagni in Mongolian Girl One Year Old, Bol. Soc. cubana pediat. **15**:51-69 (Feb.) 1943. Wylie, P. E.: Subcostosternal Diaphragmatic Hernia: Report of an Asymptomatic Case, J. Tennessee M. A. **38**:366-369 (Nov.) 1945.

TABLE 3.—*Contents of Hernial Sac by Age Groups (Decades) in 45 Cases of Subcostosternal Diaphragmatic Hernia*

Group	Age Group	Total No. of Cases	Liver Only	Omentum Only	Colon Only	Colon and Omentum	Colon and Liver	Small Bowel Only	Colon and Small Bowel	Colon and Stomach	Stomach Only	Empty
1. Children	0-12	8	2	0	4	0	1	1	0	0	0	0
2. Adults	13-29	4	0	0	1	1	0	0	1	0	1	0
	30-39	6	0	1	3	2	0	0	0	0	0	0
	40-49	3	1	1	1	0	0	0	0	0	0	0
	50-59	7	0	2	2	1	0	0	0	2	0	0
	60-69	7	0	1	1	0	0	0	1	4	0	0
	70-79	7	0	0	2	3	0	0	0	1	0	1
	80-89	1	0	0	1	0	0	0	0	0	0	0
	Not stated	2	0	0	1	1	0	0	0	0	0	0
Total †		45	3	5	16	8	1	1	2	7	1	1

† Harrington, in a recent review of diaphragmatic hernia (Monographs on Surgery, edited by B. Nolan Carter, New York, Thos. Nelson & Sons, 1951, p. 213) reports that he has operated on 14 patients with subcostosternal hernia, an incidence of 2.7% of the total 524 diaphragmatic hernias operated on by him. Excluding four cases reported by him in 1941, which presumably are included in the above 14 and which are included in table 4*B* (Cases 9, 10, 27, 34), an additional 10 cases of subdiaphragmatic hernia must be tabulated. In two the sac contained omentum only, in four colon and omentum, in three stomach and colon, and in one stomach alone plus omentum. These symptoms were not described in detail so that they cannot be included in table 4*B*.

TABLE 4.—*Symptomatology as Related to Contents of the Sac*

Case	Author and Date	Contents of Sac	Age and Sex	Side	Symptomatology: Gastrointestinal	Symptomatology: Thoracic	Symptomatology: Other	Diagnosed by	Duration of Symptoms	Comment
					A. Children					
1	Cassinelli and Tiscornia, 1947..	Colon only 4 cases	8 mo. M	Right	Vomiting, diarrhea, anorexia	Cough (dry), dyspnea, restrained respiration	.....	X-ray	4 mo.	Died; no autopsy; Mongolian idiot
2	Donovan, 1945	.....	12 yr. M	Bilateral	.....	.....	Fatigue, 1 yr.	Operation (appendectomy)	1 yr.	Asymptomatic; mentally and physically retarded
3	Valledor, 1943	.....	1 yr. F	Right	.....	Suffocation, cyanosis, intense cough	.....	X-ray	2 mo.	Treatment not given; Mongolian idiot
4	Kernau, 1940	.....	9 yr. F	Bilateral	.....	Cough	Fever	X-ray	8 yr.	Mongolian idiot; no operation
5	Eerland, 1946	Liver only 2 cases	12 yr. ..	Right	.....	Dyspnea, cyanosis	.....	Operation	12 yr.	Previous diagnosis: tetratodermoid of anterior mediastinum; multiple congenital deformities
6	Camerer, 1940	.....	6 yr. M	Right	.....	Sudden pneumonia	.....	X-ray	.....	No treatment for hernia; asymptomatic; feeble-minded
7	Donovan, 1945	Liver plus colon 1 case	16 mo. M	Bilateral	Feeding problem since birth	.....	.....	Operation	16 mo.	Only right sac with contents; Mongolian idiot; died 9 days postoperatively
8	Stobie, 1937	Small intestine only (part) 1 case	3 yr. F	Right	Chronic partial small bowel obstruction, vomiting, borborygmi	.....	Terminal spastic abdominal pain	Autopsy	3 yr.	Died (2 days after admission), partial small bowel obstruction
					B. Adults					
					Omentum Only—5 Cases					
9	Harrington, 1941	.....	64; F	Right	Intermittent stomach trouble, later vomiting and epigastric distress	.....	Loss of weight; insomnia, difficulty in swallowing, with pain	Operation	3 mo.	Previous diagnosis: peptic ulcer; two hernias (Morgagni and hiatus) discovered at operation; recovery uneventful
10	Harrington, 1941	.....	46; F	Right	.....	Productive cough, dyspnea, husky voice	.....	Operation	2 yr.	Gained 20 lb. (2 yr.); recovery uneventful
11	Meade and Ravdin, 1935.....	.....	57; F	Right	Indigestion, fullness in epigastrium with gas; increasing pain in abdomen with radiation to right shoulder	.....	Severe headaches	Operation	3 mo.	Recovery uneventful
12	Landivar and others, 1947....	.....	34; M	Right	.....	.....	.....	Operation	.....	Bronchial asthma; asymptomatic; previous diagnosis: pulmonary hydatidosis; recovery uneventful
13	Landivar and others, 1947....	.....	50; F	Right	.....	Stubborn cough; sporadic pain, right breast	.....	Operation	5 yr.	Previous diagnosis: hydatidosis; recovery uneventful
					Colon Only—12 Cases					
14	Rocha, 1944	Ascending colon	46; F	Right	Intermittent "cramplike" pain in epigastrium; "colic neurosis"	.....	.....	X-ray	2 yr.	Previous diagnosis: hydatid cyst at base of right lung; no operation
15	Thorell, 1946	"Colon"	58; F	Right	.....	.....	.....	X-ray	.....	Asymptomatic; no treatment
16	Harper Hospital, #322792.....	"Large loop of colon"	58; F	Left	Mucus in stools	Shortness of breath; palpitation of heart; gurgling in 4th left intercostal space	.....	Operation	7 mo.	Recovery uneventful

17	Althabe and others, 1944.....	"Loop of colon"	30; F	Right	Postprandial gastric distress; vomiting, nausea; sharp pain in epigastrium with radiation to right shoulder and back	.....	.....	X-ray	10 yr.	Appendectomy 9 yr. before without relief; previous diagnosis: "Gallbladder colic"; operation; recovery uneventful
18	von Greyerz, 1937.....	Transverse colon	65; M	Bilateral	.....	.....	.....	X-ray	.....	Asymptomatic; died of pernicious anemia 3 days after admission; autopsy revealed hernia
19	Bell and Heublein, 1944.....	Cecum and splenic flexure of colon	19; M	Right	.....	Cough with expectoration; slight dyspnea on exertion	.....	X-ray	2 yr.	Operation; recovery uneventful
20	Steuer, 1937	Transverse colon	75; F	Right	Distention with gas; "rumbling" in gastric region; moderate constipation	.....	Tendency toward sneezing	X-ray	1 yr.	Weight loss, 15 kg.; treatment by diet
21	Ellinger, 1939	Transverse colon	39; M	Right	.....	Slight dyspnea	.....	X-ray	.....	Previous diagnosis: emphysema; no treatment
22	Wylie, 1945	Hepatic flexure and right transverse colon	37; M	Right	.....	.....	.....	X-ray	.....	Asymptomatic; trauma 4 yr. before; no operation
23	Kratzsisen, 1921	30 cm. of transverse colon	83; M	Left	.....	.....	.....	Autopsy	.....	Asymptomatic; died of atherosclerosis, shriveled kidney, bronchitis
24	Funck-Brentano and others, 1933	10 cm.of transverse colon	70; F	Right	.....	.....	.....	Autopsy	.....	Asymptomatic; died of strangulation of transverse colon; autopsy: colon clearly gangrenous, not perforated; previous diagnosis: pneumonia
25	Curri, 1930	Colon only	37; M	Right	Gastric fullness and pressure; stools sluggish	.....	.....	X-ray	3 yr.	Intestinal paralysis 5 days postoperatively (enterostomy; resection of 32 cm. colon); complete recovery
					Colon and Omentum—8 Cases					
26	Colmers, 1941	.....	77; F	Right	Right abdominal pain	Respiratory catarrhal syndrome	.....	Autopsy	18 yr.	Died of coronary attack; previous appendectomy and later cholecystectomy without relief of pain; x-ray diagnosis: encapsulated interlobar effusion; no contrast medium used
27	Harrington, 1941	.....	34; M	Right	Gas and belching, nausea without vomiting; sharp pain in right upper quadrant; "gallstone colic"	Severe pain in chest	.....	Operation	2 yr.	Recovery complicated by bronchopneumonia (6 wk.); no recurrence of hernia
28	Parrella and Horwitz, 1949...	.....	29; M	Right	.....	Occasional pain in right chest; "fullness of neck"	.....	Operation	1 yr.	Postoperative hemothorax aspirated once; gained 38 lbs.; recovery uneventful
29	Polák and Sváb, 1947.....	.....	34; M	Left	Constipation	Continual pressure and pain beneath left costal margin	.....	Operation	2 yr.	Weight loss, 31 lb. eventual complete recovery
30	Landivar and others, 1947....	.....	72; M	Bilateral	.....	.....	.....	Operation	50 yr.	Operation for peptic ulcer; symptomatology of duodenal ulcer (50 yr.); herniation essentially asymptomatic; both sacs spontaneously reduced, empty at operation; anomaly of diaphragm noted
31	Ellinger, 1939	.....	57; F	Bilateral	.....	Bronchitis with dyspnea	.....	X-ray	.....	No treatment noted; right sac, transverse colon; both sacs, omentum
32	Hodges, 1944	.....	27; M	Right	.....	Dyspnea and general chest discomfort	.....	X-ray	11 yr.	No treatment noted

TABLE 4.—*Symptomatology as Related to Contents of the Sac—Continued*

Case	Author and Date	Contents of Sac	Age and Sex	Side	Symptomatology			Diagnosed by	Duration of Symptoms	Comment
					Gastrointestinal	Thoracic	Other			
33	Reich, 1922	.....	77; F	Right	.....	.....	.....	X-ray	.....	Asymptomatic; previous diagnosis: ovarian cystoma; no operation
34	Harrington, 1941	Colon and small intestines 2 cases	27; M	Right	Generalized abdominal pain increasing with time; nausea without vomiting; constipation	.....	.....	Operation	7 yr.	Diagnosis at operation; recovery uneventful
35	Büttner, 1941	.....	63; M	Bilateral	.....	.....	.....	Autopsy	.....	Asymptomatic patient had advanced carcinoma of rectum; immediate cause of death, circulatory insufficiency; right sac, transverse colon and omentum; left sac, small intestine
					Colon Plus Stomach and/or Omentum—7 Cases					
36	Jamain and Saks, 1940	Transverse colon, omentum, stomach	55; F	Right	Vague indigestion (4 yr.); intestinal obstruction (1 wk.), vomiting	.....	.....	Autopsy	4 yr.	Died day after admission; x-rays not taken
37	Leszler, 1941	Stomach, large intestine	65; F	Right	Complete obstruction 2 mo. previously, recurred 3 days before admission; gastric cramps; vomiting without bowel action	.....	.....	X-ray	2 mo.	Operation; recovery uneventful
38	May, 1933	Stomach, ascending colon	60; F	Bilateral	Gas pains and abdominal cramps	Occasional chest pain with increasing shortness of breath	.....	X-ray	21 yr.	Treatment refused; symptoms since an operation at age 39 for large uterine fibroid
39	Caumartin, 1948	Stomach, transverse colon, omentum	59; F	Bilateral	Sudden onset of cramping abdominal pain with nausea and vomiting (partial obstruction)	.....	.....	Operation	8 mo.	Symptoms began after ileotransverse colostomy and resection of ascending colon for carcinoma; recovery from herniorrhaphy uneventful
40	Saltzstein, Linkner and Scheinberg, 1949	Transverse colon, stomach (⅔) omentum	68; M	Right	Pyloric obstruction with vomiting and epigastric distress (2 days)	Chronic cough (8 yr.)	.....	Operation	8 yr.	Previous diagnosis by x-ray: bronchiogenic carcinoma of right lung; preoperative alkalosis responded to potassium therapy; recovery uneventful
41	Ellinger, 1939	½ stomach, transverse colon, omentum	66; F	Right	Severe gastric cramps with profuse vomiting (complete obstruction)	.....	.....	X-ray; autopsy	2 yr.	Diagnosis 2 yr. previously without stomach in sac, asymptomatic until stomach involved, then obstruction; died in 3 days
42	Sielmann, 1924	Stomach, transverse colon	71; F	Right	Gastric pain after meals, constipation	Pain in cardiac region; dyspnea	Frequent attacks of dizziness	X-ray	.....	No operation; frequent attacks of pneumonia when a child
					Miscellaneous—3 Cases					
43	Kaiser, 1940	Stomach only	23; M	Right	.....	.....	.....	X-ray; operation	.....	Asymptomatic; hernia discovered at army induction; operation; recovery uneventful
44	Reich, 1922	Liver only (all or part)	47; M	Right	Peptic ulcer symptoms	.....	.....	X-ray	.....	Asymptomatic; discovered in routine chest plate; no operation and no treatment
45	Büttner, 1941	Empty	71; M	Bilateral	.....	.....	.....	Autopsy	.....	Asymptomatic; autopsy showed "multiple adipose tumors"; herniations due to tumors; cause of death not stated

In one of these the age was given as 23 years. In two other cases, the age was not stated. We have arbitrarily placed these two cases in this age group. In 31 of the cases the condition occurred in persons from 30 to 80 years old, with 22 of the 37 adult patients, or 59%, over 50 years of age.

The contents of sac in the adult patients can be classified thus: (*a*) omentum only, 5 cases; (*b*) colon only, 12 cases; (*c*) colon and omentum, 8 cases; (*d*) colon and small bowel, 2 cases; (*e*) colon and stomach, 7 cases; (*f*) stomach alone, 1 case; (*g*) liver only, 1 case, and (*h*) empty, 1 case.

As can be seen from Table 3, in 33, or 73% of the 45 cases reported, the colon, with or without other viscera, was involved in the hernia. The cases in which the sac contained colon only ranged through the entire age period from infancy to old age. In an infant, the sac is apt to contain the liver but not stomach or omentum. In an adult, the liver usually does not enter the sac. Those patients who had hernias involving the colon and stomach were all in the older age group, over 50 years. The stomach alone was found in the sac in one patient, aged 23, but the report is based on only a routine roentgenogram of the chest from an induction center.

SYMPTOMS IN GROUP 2

The contents of the sac determine the symptoms, which are referred either to the chest or to the gastrointestinal tract.

Omentum Only.—When only the omentum was in the sac (five cases), the chest symptoms were difficulty in swallowing, husky voice, stubborn cough, or sporadic pain in the right chest. Abdominal symptoms in this group were intermittent stomach trouble, indigestion, feeling of fulness with gas, and pain in the abdomen radiating to the right shoulder. These symptoms were, for the most part, of long duration—two to five years. All five patients with omentum only in the sac were operated on. Two had had a previous diagnosis of pulmonary hydatidosis. One had been treated for four years for peptic ulcer (Case 9). Ulcer was found at operation in addition to the hernia. One patient had a preoperative diagnosis of gall bladder disease; at operation none was found. The fifth patient underwent exploratory laparotomy. In 4 of the 5 cases the hernia was discovered at the operation. Operative recovery was uneventful in all.

Colon Only.—When only the colon was in the sac (12 cases), the duration of the symptoms ranged from seven months to ten years. Three patients showed chest symptoms only: cough, dyspnea, shortness of breath, palpitation of the heart, cough with expectoration, and dyspnea on exertion. These three patients had no abdominal symptoms. Four had abdominal symptoms and no chest symptoms, chiefly postprandial gastric distress, nausea, distention, rumbling in the abdomen, borborygmi, and moderate constipation. Neither constipation nor vomiting was a prominent symptom in this group. Only two of these patients had any sharp pain in the epigastrium. Five of the 12 were asymptomatic; this is remarkable, for most of them had a large loop of colon resident in the sac. Three of these hernias were disclosed by x-ray examination, and two were found at autopsy. The antemortem diagnosis in one of these was pneumonia. Autopsy showed a gangrenous loop of transverse colon in the hernia as the sole abdominal contents, while the lungs were normal. In 9 of the 12 cases the hernia was discovered by x-ray examination. In 4 of the 12 cases an antecedent diagnosis other than diaphragmatic hernia had been

made, namely, hydatid cyst at the base of the right lung, "gall bladder colic," emphysema, and pneumonia. In only four cases was an operation performed; all the patients recovered completely. In one, 32 cm. of colon was resected.

Colon and Omentum.—In seven cases the sac contained colon and omentum. The most constant symptoms were related to the chest, all but one of the patients reporting chest pain, dyspnea, and bronchitis. Three of the patients had abdominal symptoms in addition. In one case the hernia was discovered during an operation for duodenal ulcer; ulcer was also present. In another case the hernia was discovered at an operation for gallstones. No stones were found, but the transverse colon and omentum were found in the subcostosternal sac. One patient had had abdominal pain for 36 years, unrelieved by appendectomy and cholecystectomy. At age 59, she had bronchitis and marked dyspnea. A roentgenogram showed a shadow in the right lower pulmonary field diagnosed as encapsulated interlobar effusion. Autopsy, at age 77, showed transverse colon, omentum, and round ligament in the chest. Three of eight patients were operated on, all successfully.

Colon and Small Bowel.—There were two cases reported in which the colon and part of the small intestine were found in the sac; both patients were adults. Of these, one was asymptomatic, the hernia being discovered at autopsy. In the other case the hernia was discovered in an exploratory operation, the symptoms being increasing abdominal pain, nausea without vomiting, and constipation. The repair was made, and the recovery was uneventful. There were no chest symptoms in either of these two cases.

Colon and Stomach.—As noted, we found seven cases in which the stomach in addition to the colon was in the chest. The youngest of the patients was 55 years old. Evidently, the sequence is that the colon may be resident in the sac for some time, often producing very few symptoms (mild abdominal distress, gas, constipation, no obstruction) and then suddenly for some reason the hernia mouth dilates and the stomach slips up. In five of these cases with stomach and colon in the sac, there was sudden obstruction with vomiting, severe abdominal and epigastric pain, and no bowel movements. Unless the condition is remedied immediately, death ensues from pyloric obstruction and its sequelae. Chest symptoms are minimal in this group (in three cases there were chronic cough, occasional chest pain, and dyspnea). Of the five patients in whom obstruction was manifest, three were operated on; all recovered completely. The fourth patient died after intestinal obstruction symptoms of one week's duration. He had had vague indigestion for four years. Autopsy showed stomach, transverse colon, and omentum in the chest. In the fifth case, the diagnosis was first made by x-ray examination when the hernia was asymptomatic; at this time transverse colon and probably a portion of the omentum were in the sac. Two years later the patient was admitted to the hospital with acute intestinal obstruction. He died in three days. Autopsy showed one-third of the stomach (greater curvature), plus a 20 cm. loop of transverse colon, and part of the omentum in the sac.

Stomach Alone.—The one case in which stomach alone was the sole contents of the sac (Fig. 4) was reported briefly and no symptoms were detailed.

Liver Alone.—In only one adult was the liver alone involved in the hernia. The patient was asymptomatic, the hernia being discovered by x-ray, during a routine gastrointestinal series for bleeding duodenal ulcer. There was a "dense shadow

extending from the right diaphragm into the right lower lung field, the size of a fist. Anterior view showed it close to the anterior thoracic wall. It was homogeneous and of the same density as the liver shadow." A gastrointestinal roentgenogram showed that there was no malposition of the intestine. No treatment was given. The author's diagnosis was right parasternal diaphragmatic hernia containing liver, dense shadow and absence of hollow viscera in the hernia site.

TABLE 5.—*Operations Performed in 21 Cases of Subcostosternal Hernia*

Age	Case	Preoperative Diagnosis	Operative Findings (Contents of Sac)	Result
12	2	Appendectomy	Appendicitis (colon)	Complete recovery
12	5	Teratodermoid of anterior mediastinum	Liver	Complete recovery
16 mo.	7 M	Morgagni hernia	Liver and colon	Died 9 days postoperatively (bronchial pneumonia)
64	9	Tumor at base of right lung and hiatus hernia	Omentum	Complete recovery
46	10	Probable tumor (chest)	Omentum	Complete recovery
57	11	Pulmonary cyst	Omentum	Complete recovery
34	12	Pulmonary hydatidosis	Omentum	Complete recovery
50	13	Hydatidosis	Omentum	Complete recovery
58	16	.....	Colon	Complete recovery
30	17	Gallstones and diaphragmatic hernia	Colon	Complete recovery
19	19	Morgagni hernia	Colon	Complete recovery
37	25	Morgagni hernia	Colon-resection 32 cm. large intestine	Intestinal paralysis 5 days postoperatively; eventual complete recovery
34	27	Morgagni hernia	Colon and omentum	Bronchial pneumonia of 6-wk. duration; eventual complete recovery
29	28	Morgagni hernia	Colon and omentum	Complete recovery
34	29	Morgagni hernia	Colon and omentum	Postoperative hemothorax aspirated once; otherwise complete recovery
72	30	Duodenal and pyloric ulcer	Ulcer found plus Morgagni hernia (spontaneous reduction at operation)	Complete recovery
27	34	Morgagni hernia with partial obstruction	Colon	Complete recovery
65	37	Morgagni hernia with partial obstruction	Stomach and colon	Complete recovery
59	39	Morgagni hernia with partial obstruction	Stomach, colon, and omentum	Complete recovery
68	40	Bronchiogenic carcinoma of right lung	Stomach, colon, and omentum	Complete recovery
23	43	Diaphragmatic hernia of right side (abdominal exploratory)	Stomach	Complete recovery

In one autopsy report it was stated that both sacs of a bilateral Morgagni hernia were empty. The presumption was that spontaneous reduction occurred at or immediately before death.

One sac was empty.

Table 5 is a summary of the 21 operations performed in this total series. There was one death, that of an infant 16 months old. Evidently, the problem of substernocostal hernia is one chiefly of diagnosis.

REPORT OF A CASE

S. D., aged 68, was admitted to Harper Hospital on Sept. 25, 1949, referred by Drs. Willard Mayer and Max Beitman.

Past History.—The patient had been in relatively good health all his life. In 1941 a chronic cough had developed, which he attributed to smoking. It was not related to eating or to change in body position. During a routine general physical check-up at that time, a roentgenogram of the chest revealed a "peculiar density with an area of decreased density in the base of the right lower lobe of the lung." The physical findings at that time were essentially negative. Both lung fields were normal on auscultation and percussion. He was advised to spend the winters in Florida, which he has done. The cough disappeared in two months.

In 1945 a routine check-up showed the same x-ray findings in the chest. Bronchoscopy showed a narrowing of the secondary divisions of the right lower lobe bronchus. A diagnosis of bronchogenic carcinoma of the right lung was considered. Nevertheless, he has been entirely asymptomatic until this present episode. He had been constipated for years but was no worse during the past year and he had no constipation while in Florida. There was no return of the cough which he had had in 1941. There had been no weight loss (his usual weight was 131 lb. [59.4 kg.]). There was no epigastric distress or heartburn.

Present Illness.—On the afternoon of Sept. 21, 1949, he painted his porch. After one and a half hours of work, while bending over, he suddenly experienced a sharp epigastric and substernal pain. This radiated to the right costal and lower chest region. It persisted for only a few minutes, and he resumed his painting. That evening, after a heavy dinner, there was a sensation of fulness in the substernal region and chest for 10 minutes, followed by vomiting. The vomitus consisted of his dinner, mostly undigested food. He felt better, the epigastric distress subsided, and there was no further pain. However, he continued to vomit intermittently for the next four days up to the time of his admission. The vomiting occurred chiefly after meals and was profuse each time. "He could not keep anything down." There was very little discomfort accompanying it. There was no hematemesis or melena. During these four days there were no bowel movements and no passage of flatus. The vomitus was not fecal. He remembered little except the continued vomiting. There were no other significant referable symptoms.

Physical examination showed a well-developed and well-nourished elderly white man lying quietly in bed and apparently in great distress. He was confused and disoriented but not in stupor. There was marked dehydration. The lips and finger nails were cyanotic. The temperature was 97.6 F, the pulse rate 100, respiratory rate 24, and blood pressure 120/90. The heart was not enlarged. The point of maximal impulse was in the fifth intercostal space 7.5 cm. from the midsternal line. A loud, harsh, nontransmitted, systolic murmur was heard, with greatest intensity at the apex.

The lungs were normal on auscultation and percussion. The abdomen was flat and soft. A succussion splash was evident in the upper midabdomen near the left costal margin. Peristaltic sounds were normal. The kidney, liver and spleen were not palpable. No masses were felt.

The stomach was aspirated and 2,200 cc. of clear fluid withdrawn. The patient immediately felt much better, but his mental condition continued to deteriorate. There were increased disorientation, confusion, and, at times, delusions. His condition now appeared critical.

Laboratory data on September 26 were as follows (Fig. 1): The red blood cell count was 5,820,000; hemoglobin, 17.5 gm. (114%); white blood cell count, 18,700; nonprotein nitrogen 173.5 mg. per 100 cc., and carbon-dioxide-combining power, 103 vol. %. The urine showed a few red and white blood cells and granular casts; the urine output was 450 cc. in 24 hours.

There were thus marked hemoconcentration, marked alkalosis, and severe azotemia. A flat plate study of the abdomen next day (September 27) revealed nothing remarkable. There were no distended loops of small or large bowel. An x-ray picture of the chest showed "a concave shadow of increased density in the right lung base extending from the right mediastinal margin to the axillary wall, just above the diaphragm. Beneath this there is a collection of gas" (Fig. 2).

A Levin tube was passed and the stomach emptied. Under fluoroscopy the tube was seen to be passing from the stomach in the upper left abdomen through a defect in the diaphragm into the right lower thoracic cavity. Thirty cubic centimeters of barium sulfate injected through

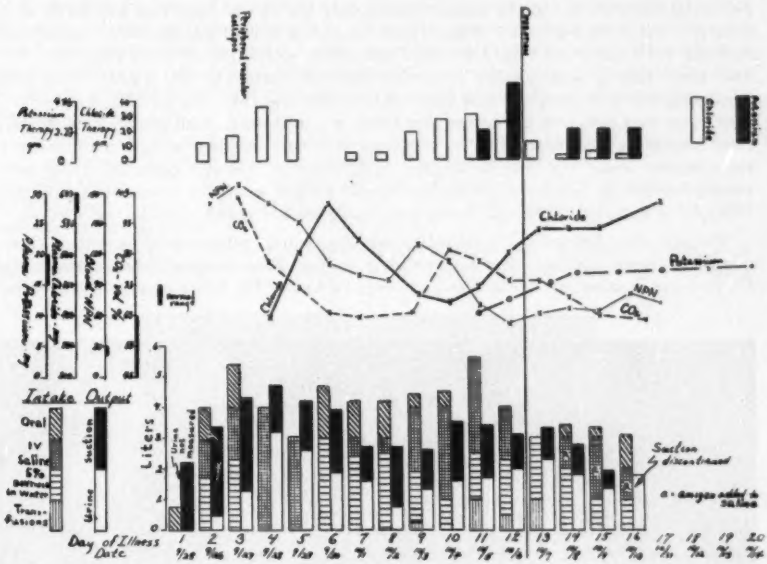

Fig. 1.—Clinical course of patient.

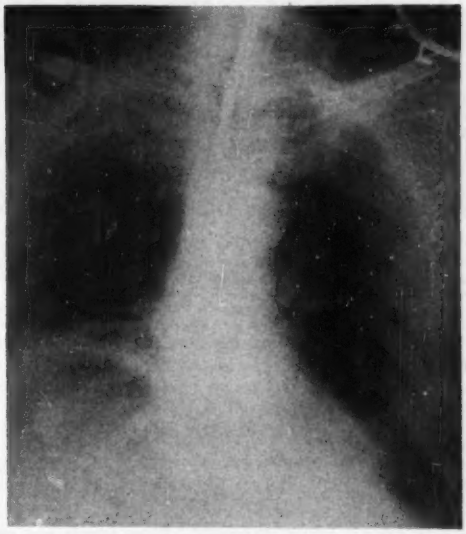

Fig. 2.—Roentgenogram made on day after admission (Sept. 27, 1949). There is an area of increased density in the right lung base extending from the right mediastinal margin to the axillary wall, just above the diaphragm. Beneath this there is a collection of gas.

the Levin tube showed that the stomach was greatly dilated and more than two-thirds of its distal part was in the right chest (Fig. 3*A*). A lateral film showed that the defect was anterior, overlying the dome of the liver, and it was immediately subcostosternal in location (Fig. 3*B*). Two hours later a small amount of barium was still retained in the stomach. The chest roentgenograms were compared with those taken in 1941 and 1945. The peculiar density in the right lower lung field with the rarified area below it was identical in all roentgenograms; they could almost be superimposed. The diagnosis was now evident: a right subcostosternal diaphragmatic hernia (through the foramen of Morgagni or Larrey's space, also called parasternal, retrosternal, anterior diaphragmatic hernia) through which the stomach had protruded. The pylorus had suddenly become obstructed, causing marked gastric retention and alkalosis.

The next day (September 28) the patient was disoriented, confused and in a state of stupor. Continuous Levin tube suction was immediately started. Four thousand cubic centimeters of 5% dextrose in saline was given during the next 24 hours. The following day he was better.

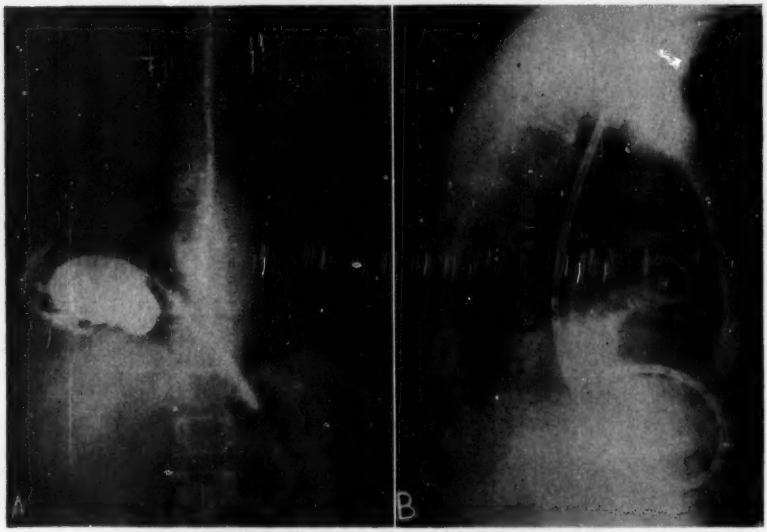

Fig. 3.—*A*, Levin tube passed into the stomach, then through a defect in the diaphragm and into the right lower thoracic cavity. Thirty cubic centimeters of barium introduced into the Levin tube outlines two-thirds of the stomach in the right chest. *B*, lateral roentgenogram. Defect is in anterior portion of the chest cavity.

The confusion and disorientation were completely gone, and he was alert and responsive. The laboratory data also showed improvement, as follows: Chlorides were 500.18 mg. per 100 cc., carbon dioxide-combining power was 74.5 vol. %, and nonprotein nitrogen 150 mg. %. The urine output was 3,250 cc. in 24 hours.

For the next four days he continued to improve. He was allowed up. The Levin tube was clamped, and it appeared that the pylorus was open, because a small amount of bile-colored fluid was returned through the tube. Liquids were allowed orally. His urinary output was adequate.

On October 2 the patient was up and ambulatory, taking liquids well and had had a bowel movement. The nonprotein nitrogen was now 93.7 mg. per 100 cc.; chlorides, 586 mg. per 100 cc., and carbon dioxide-combining power, 64 vol. %.

It was thought that a few more days of treatment would cause the nonprotein nitrogen level to drop further and he would be able to withstand an operation. A flat plate of the abdomen at this time revealed that the barium sulfate which had been injected through the Levin tube five days before now outlined the hepatic flexure and transverse colon. To our surprise, these portions of the colon were in the right thoracic cavity along with the distal two-thirds of the stomach (Fig. 4).

The next night the nurse noticed that the patient was restless, unable to sleep, appeared tired and exhausted and at times was lethargic. His skin was cool and moist, and he was perspiring freely. At 5:30 a. m. he suddenly went into a state of severe peripheral collapse. He was deeply cyanotic, cold, and clammy, with rapid thready pulse (140), and the blood pressure dropped to 70/40.

The heart rhythm for the first time showed a premature beat. Myocardial infarction or pulmonary embolus was seriously considered. Administration of blood plasma was immediately

Fig. 4.—Flat plate of the abdomen taken five days after introduction of 30 cc. of thin barium mixture into the Levin tube. Levin tube is in the stomach, which is in the right lower chest. Barium outlines hepatic flexure and transverse colon in right chest, apparently surrounding the stomach.

started. He improved only slightly, and at 11:00 a. m. he was still in a state of shock. The blood pressure was 80/40. He had again gone into severe alkalosis. Laboratory examination (Oct. 3, 1949) showed chlorides 432.9 mg. per 100 cc., nonprotein nitrogen 138 mg. and carbon dioxide-combining power 65 vol. %.

The remainder of the day he was given 2,500 cc. of 5% dextrose in saline, but despite this the plasma chlorides the following morning fell to 421 mg. per 100 cc., the carbon dioxide-combining power rose to 86 vol. %, and the nonprotein nitrogen fell to 110 mg. His urinary output was 875 cc. in 24 hours. Blood pressure remained around 90/50. The electrocardiographic report was normal except for frequent auricular extrasystoles. The patient was still critically ill and, in spite of enormous quantities of saline, the alkalosis coud not be corrected.

On this date (October 4) the blood serum potassium was determined. It was low—10.3 mg. per 100 cc. (normal, 16 to 22 mg.). He was immediately given 3,000 cc. of 5% dextrose in saline intravenously, which contained 2.23 gm. of potassium chlorides per liter (Randall and Lockwood). The response was dramatic. Within a few hours he no longer felt weak and exhausted. His skin was warm, and the cyanosis disappeared. The blood pressure rose to 104/70. The 24-hour urinary chloride level fell to 1 gm., and his urinary output increased from 875 to 1,675 cc.

On October 5, 2,000 cc. of 5% dextrose in water, with 2.23 gm. of potassium chloride in each bottle, was given intravenously. He was no longer in shock but rather was alert, bright and responsive. His general condition appeared excellent. The blood pressure was 130/70, better than at any previous time in the hospital. Urinary output was 2,050 cc. Chemical examination of the blood gave the following data: The nonprotein nitrogen was 56.3 mg. per 100 cc., the lowest since admission. Chlorides were 500.8 mg. per 100 cc., and the carbon dioxide-combining power was 76 vol. %.

On October 6 the Levin tube was clamped and an attempt at feeding was made, which was immediately followed by vomiting and gastric retention. Apparently, with both the stomach and the colon crowded through the hernia opening into the right chest, some passage of gastrointestinal fluids was possible, but the slightest distention, or perhaps edema, of the stomach walls caused obstruction. Although the chemical balance was not entirely corrected, it was thought that his condition would now withstand surgery and that it would be unwise to delay further.

On Oct. 7, 1949, abdominal exploration was done through a right rectus incision. There was a large fist-sized hernial defect in the diaphragm immediately above the dome of the liver. The transverse colon had herniated through this large defect just posterior to the xiphoid process and the right costal margin. Approximately 7 in. (18 cm.) of the colon was above the diaphragm and in the right thoracic cavity. The colon was reduced by careful traction. It was not adherent anywhere; however, the colon that was contained in the hernial sac appeared slightly edematous and swollen. After the transverse colon was delivered and mobilized out of this hernial defect, the omentum followed. The entire omentum was found lying in the right chest. It was thickened and showed signs of chronic inflammatory reaction. After the delivery of the omentum, the stomach was found to be lying in the right chest above the liver. Approximately two-thirds of the stomach was above the diaphragm, extending from the pylorus 5 to 6 in. (13 to 15 cm.) toward the cardia. The duodenum was so elongated that it could be brought out onto the surface of the abdomen. After the abdominal viscera were delivered, the defect in the right diaphragm admitted half a fist, and the upper limit alongside the right mediastinum could just be reached with the finger. It was lined with a well-defined and peritonealized sac. The edges were quickly freshened and rapidly brought together. The abdomen was closed.

The patient had a totally uneventful postoperative course. He was maintained on potassium chloride intravenously (2.23 gm.) daily until Oct. 11, 1949. He then began taking nourishment orally. On October 11 the blood chemistry data were as follows: chlorides, 584 mg. per 100 cc.; nonprotein nitrogen, 69 mg.; potassium, 14.64 mg.; carbon dioxide-combining power, 63 vol. %, and protein, 6.17 mg.

On October 14 the serum potassium was 17.78 mg. per 100 cc. The patient was eating well, and bowel movements were normal. He was discharged on October 22.

When last seen, on Aug. 8, 1950, he had regained his preoperative weight (131 lb. [59 kg.]), had no complaints and looked the picture of health.

Summary of Case Report.—The colon had evidently been present in the sac for some years (certainly as long as eight years), for a reevaluation of the chest roentgenogram taken at that time showed gas containing right lower chest shadows. There were very few symptoms, mild cough and no gastrointestinal symptoms. After sudden exertion four days before the patient's admission to the hospital which involved bending forward, pyloric obstruction developed, with severe alkalosis and hypochloremia. This was refractory to large quantities of saline and progressed to the point of peripheral circulatory collapse, with cyanosis and a blood pressure drop

to 70/40. Potassium chloride given intravenously immediately reversed this state of shock and transformed a critical and almost terminally ill patient to one who withstood surgery.

This condition has become more clearly recognized recently under such terms as "refractory alkalosis," and "alkalosis with hypochloremia and hypokalemia." According to several authors, it is actually a potassium deficiency.

At operation a large fist-sized right subcostosternal diaphragmatic hernia was found, containing 7 in. (18 cm.) of transverse colon, the entire omentum and the distal two-thirds of the stomach. The contents were easily replaced into the abdomen, the hernia sac repaired quickly and the abdomen closed.

SUMMARY AND CONCLUSIONS

A case of subcostosternal diaphragmatic hernia containing stomach, omentum and colon is described. Forty-four other cases of this type of hernia have been collected from the literature and the symptomatology reviewed.

The incidence of subcostosternal hernia is 2.6% of all diaphragmatic hernias.

Eight of the total 45 cases occurred in children 12 years of age and younger. In this age group the sex incidence is equal. In early adult years (before 40) there are relatively few (six) cases and males predominate. After that there is an increasing number of cases, and after age 50 there are two and a half times as many females as males. Among the eight patients in early life, there were four Mongolian idiots, two feeble-minded patients, and one other with congenital defects. There were no such congenital abnormalities in the adult cases.

In infancy and childhood, the liver has been found turned upward into the sac. In childhood the liver is thin, elongated, and somewhat mobile. No adult hernias contained the liver (with one exception, case 44). By contrast, no hernias in infants or children contained omentum, which is apparently too thin and immature in early life. The stomach also was not found in the hernias in children.

The colon was resident in the sac in all age groups and in 73% of the total 45 cases. The presence of colon causes mild abdominal symptoms, i. e., lower abdominal distress, gas, and mild constipation, but never obstruction. Frequently it is asymptomatic.

In adults the omentum may be the sole contents of the sac (five cases). The symptoms may be chest pain or cough, with a persistent shadow in the right lower region of the chest which has been interpreted as hydatidiform disease or empyema.

The stomach enters the sac only after the colon has been in it for a long time, usually several years. Cases in which this occurs are the only ones in which sharp and sudden obstruction is encountered. Unless the condition is immediately remedied, death ensues from pyloric obstruction and its sequelae.

By and large, operations for the cure of hernias were successful and convalescence uneventful. The chief problem is that of diagnosis. Some hernias were asymptomatic and were discovered on routine x-ray examination of the chest, at operation for other conditions, or at autopsy. All hernias of the Morgagni type should be operated on. In addition to the usual reasons for repairing such abnormal openings, there is the danger of the stomach entering the sac later in life and causing sudden pyloric obstruction.

SURGICAL MANAGEMENT OF MASSIVE HEMORRHAGE FROM PEPTIC ULCER

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DURING the past 10 years the articles appearing in the medical literature on the subject of massive hemorrhage from peptic ulcer have been numerous, but rather contradictory.[1] The policies advocated have ranged from nonoperative treatment regardless of circumstances to the opposite extreme of operation on all patients actively bleeding from a peptic ulcer. In 1946 [2] Heuer reported the experience of this clinic with 337 patients admitted in a 14-year period (1932 to 1946) for massive hemorrhage believed due to a peptic ulcer. His review brought out the fact that the mortality rate for the group operated on immediately was only 10%, whereas for those operated on after hemorrhage for 48 hours or longer the mortality rate rose to 70%. He concluded that if operation was to save life it should be undertaken within 48 hours. He also stressed, however, that 288 of the 337 patients, or 85.5%, recovered without immediate or early operation. Careful and concise reports at reasonable intervals from the many clinics throughout the country should make a fair cross section of current practice available and would indicate which policy offers the most to these patients. Our purpose here is to describe our present methods of management in this situation, together with immediate and early results in a series of 58 patients admitted to the surgical pavilions of this center over a period of four years, 1946 to 1949. During this four-year period, a total of 414 patients with peptic ulcer was subjected to surgical treatment of a definitive nature. This larger series has been reviewed elsewhere.[3]

From the Department of Surgery of The New York Hospital—Cornell Medical Center.

1. Bockus, H. L.: Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1943, Vol. I, pp. 597-599. Lewison, E. F.: Collective Review: Bleeding Peptic Ulcer, Internat. Abstr. Surg. **90**:1-30, 1950, in Surg., Gynec. & Obst., Jan., 1950. Wechsler, L., and Odle, S. G.: The Management of Profuse Bleeding from Peptic Ulcer, Am. J. Digest. Dis. **17**:276-280 (Aug.) 1950. Best, R. R.: The Consideration for Surgery in the Management of Bleeding Peptic Ulcer, Nebraska M. J. **35**:11-15 (Jan.) 1950. Welch, C. E.: Treatment of Acute, Massive Gastroduodenal Hemorrhage, J. A. M. A. **141**:1113-1119 (Dec. 17) 1949. Holloway, J. B.; Armur, T., and Proctor, W. H., Jr.: Management of Bleeding Peptic Ulcer, Arch. Surg. **61**:487-498 (Sept.) 1950. Stewart, J. D.; Schaer, S. M.; Potter, W. H., and Massover, A. J.: Management of Massively Bleeding Peptic Ulcer, Ann. Surg. **128**:791-802 (Oct.) 1948.

2. Heuer, G. J.: The Surgical Aspects of Hemorrhage from Peptic Ulcer, New England J. Med. **235**:777-783 (Nov. 28) 1946.

3. Glenn, F.: Present Status of the Surgical Treatment of Peptic Ulcer, J. A. M. A. **145**:790-794 (March 17) 1951.

SYMPTOMS

The criteria for our diagnosis include a hemoglobin concentration of 10 gm. per 100 cc. or less and a red blood cell count of less than 3,700,000 per cubic millimeter in the presence of clinical manifestations of bleeding from a peptic ulcer. Forty-two of the 58 massive bleeders, or 72.4%, were men and 16, or 17.6%, were women, a typical sex ratio for peptic ulcer. The average age of the group was 52.6 years, placing many of them in the upper age bracket.

We believe it to be of some significance that 50 in the group, or 86.2%, had had epigastric pain for more than a week prior to admission to the hospital. Most of the patients had received conservative treatment for the ulcer at one time or another. Thirty-one, or 62%, gave a history of recurrent pain for one to 10 years, and eight patients, or 16%, had had episodes of ulcer pain for more than 15 years. Twenty patients, 34.8%, gave a history of vomiting at one time or another, 15 reporting occasional minor episodes and 5 moderate to severe attacks. At the time of admission, partial obstruction was noted to be present in two of these patients and complete obstruction in one. Forty of the 58 patients were found to have duodenal ulcers; 11 had gastric ulcers; 5, marginal ulcers; 1, a pyloric ulcer, and 1, both duodenal and a gastric ulcer.

In four patients, 6.9%, bleeding had been the first symptom, and in four others pain, nausea, vomiting, and bleeding had persisted for a week prior to admission. Twenty-four patients, 41.4%, had had hemorrhage on previous occasions and gave a combined history of 61 episodes of distinct and unequivocal bleeding. Twenty-five of the episodes were considered to have been massive hemorrhage, while the other 36 instances were deemed to have been of less extent.

Twenty-nine patients, or half of the 58 bleeders, had had 41 previous operations, 10 of which were for the ulcer condition. Six had had gastroenterostomies; one, a subtotal gastric resection, and three, plications for a perforated duodenal ulcer. Eight appendectomies and six cholecystectomies were also among the 41 previous operations and in some instances may have been done for symptoms due to the ulcer.

On admission, 49 of the 58 bleeders, 84.5%, were in good or fair condition. Four patients were in poor condition, and five were in shock. Fourteen entered the hospital within eight hours of onset of hemorrhage, while the remainder waited until some time later. One patient gave a history of three weeks of intermittent bleeding prior to admission. Forty-seven of the 58, 81%, had a hemoglobin concentration of less than 10 gm. per 100 cc., and 50, or 86.3%, had a red blood cell count of less than 3,500,000. The remainder with higher counts either continued to bleed with a concomitant fall in blood count or were dehydrated. After hydration they demonstrated a corresponding drop in hemoglobin concentration and red blood cell count, thus falling into our classification of patients with massive hemorrhage.

TREATMENT

Conservative treatment was instituted on admission, with one exception. Fifty-two patients were given nothing by mouth and fluids by clysis; observations every half-hour and frequent blood counts were made; morphine sulfate was administered every four hours if respirations were over 14; rest in bed was maintained, and

multiple small blood transfusions were given. After the data collected indicated that the patient had ceased active bleeding, administration of 30 cc. of milk and cream every hour and of antacids, phenobarbital, and belladonna was started. The diet was then gradually increased over a period of five or six days to a six-feeding soft peptic-ulcer diet. When symptoms appeared controlled, diagnostic procedures were carried out to confirm the diagnosis of peptic ulcer. These included a gastrointestinal series done with minimal manipulation. One patient was given a continuous intragastric drip on admission, and administration of a six-feeding soft peptic-ulcer diet was started for three other patients. Their bleeding ceased and did not recur prior to operation. One patient was started on a milk-cream regimen on admission, but hemorrhage occurred again on his sixth hospital day. One patient was in shock on admission, having bled repeatedly from a known duodenal ulcer. He was, therefore, prepared for immediate operation.

As shown in the following table, 46 of the 58 patients, or 79.3%, stopped bleeding within 48 hours after admission. One patient maintained a low blood count for eight days after admission, despite transfusion, indicating a persistent and

Massive Hemorrhage from Peptic Ulcer: Occurrence in The New York Hospital, 1946 to 1949

Duration of Bleeding After Admission, Days	No. of Patients
Immediate operation	1
1	36
2	10
3	3
4	4
5	2
6	1
8	1
	58

continuous loss of blood, even though small, but the patient's condition did not approach a state of shock.

The common conditions that require differential diagnosis in patients with massive hemorrhage from the upper gastrointestinal tract are esophageal varices, tumors, diverticula, or ruptured arteriosclerotic aneurysmal dilatations arising from the stomach or occasionally from the esophagus. When a positive diagnosis cannot be made, but the patient continues to bleed despite a reasonable attempt at conservative management, the operating room is made ready while he is taken to the x-ray room for examination of the upper gastrointestinal tract. If an ulcer is demonstrated, or if presumptive evidence of such is found, the patient is taken directly to the operating room.

Five of our 58 patients continued to bleed after admission. Seven others gave clinical evidence that they had stopped bleeding before admission, but hemorrhage started again while they were receiving conservative treatment. Only 13 emergency procedures were necessary for the group of 58 patients, including the patient operated on immediately after admission. Thus, from our experience, we feel that in most cases of massive hemorrhage from a peptic ulcer operation may be delayed after admission until such time as the patient is in a better condition to withstand the procedure. But this policy is not considered sound unless the patient is kept under constant and critical surveillance and operated on when it appears that

further conservative treatment may prove hazardous. There is a great difference between this attitude and that which favors operation for all patients with massive bleeding, or that which reserves operation as a final resort when the patient is moribund.

There are two important aspects to the problem that confronts the clinician who has a patient bleeding from a peptic ulcer. The first is to determine the rate of bleeding, and the second is to decide when the patient has stopped bleeding. With regard to the first, we can, to an extent, estimate the rate of bleeding by noting how much blood is required to restore and maintain the pulse rate and blood pressure at normal range for a specific time. Special studies were done on our series for blood urea nitrogen and serum protein levels, with the hope that they would prove to be of diagnostic value, but such was not the case. The blood urea nitrogen level dropped significantly 4 units or more in 28 cases, 48.3%, but it often became elevated first because of dehydration, and its subsequent fall corresponded to rehydration rather than to cessation of bleeding. The serum protein determinations were, for the most part, noncontributory. The blood volume measurements done on several patients were of little more value than the hematocrit readings. Reactions to all these tests were indicative of the rate of bleeding, but they were not sufficiently quantitative to be considered specific or to justify an opinion that the bleeding had ceased. Results of these tests are best used in conjunction with the clinical course as a basis for therapy.

When ordering preoperative medication for a patient with bleeding ulcer, it is better to prescribe undersedation than oversedation. Too much preoperative medication may lead to vascular collapse during operation. Use of morphine sulfate or meperidine (demerol®) hydrochloride should be limited preoperatively because of the depressive action of the drugs. In regard to anesthesia, ether and cyclopropane were the agents used most frequently in our series, having been employed for all but three of the 58 patients. Thiopental (pentothal®) sodium is used for induction, followed by administration of ether or cyclopropane, unless some unusual contraindication requires employment of another type of anesthetic agent. When given with an adequate amount of oxygen, both ether and cyclopropane are safe for those in serious condition, and at the same time they provide satisfactory abdominal relaxation for the surgeon.

The Polya operation was the most-used type of procedure, being employed in 37 patients, or 63.8%. We do not combine vagotomy with gastric resection routinely, but the combination was used in two patients of this series. Whether to remove the ulcer in a patient who is still bleeding may be a difficult problem. It should be decided according to the particular case and not by strict adherence to a general policy. In instances of active bleeding calling for an emergency procedure, we have observed that mere identification and ligation of the bleeding vessel, leaving the ulcer intact, has sometimes been followed by hemorrhage from the same area later. Therefore, we feel that in such a situation the ulcer should be removed. Patients who have stopped bleeding and for whom surgical treatment is more or less elective present a somewhat different problem. Here, it is preferable to remove the ulcer, but not if such removal is likely to render closure of the duodenal stump hazardous or injure the common duct and adjacent structures. If the latter are in

danger, removal of the ulcer is probably more hazardous than the likelihood of bleeding from the ulcer itself after gastric resection. We believe that if the ulcer can be removed safely it should be removed.

POSTOPERATIVE CARE AND COMPLICATIONS

Postoperative care follows the same regimen as for any gastric resection. A Levin tube is attached to gentle suction for 48 hours, after which the patient is started on a progressive peptic-ulcer diet. Antimicrobic drugs are given routinely, and fluid intake is maintained by intravenous administration of solutions. Care is taken to ambulate the patient on the day of operation, and early and vigorous respiration exercises are encouraged. If a sedative is given 20 or 30 minutes before ambulation or forced coughing, the patient will be much more comfortable and cooperative.

Two patients died from postoperative complications; 18 had 25 nonfatal complications. The mortality rate of 3.5% is higher than that for the total number of patients who underwent gastric resection for peptic ulcer during this same period; for a group of 318 patients the mortality was 1.5%. Ten of the 25 nonfatal complications were directly related to the procedure. Half consisted of postoperative gastric retention, or the so-called ninth-day disease, for which no satisfactory explanation has yet been found. Two patients were believed to have bled postoperatively from the anastomosis, since the ulcer had been removed in both cases. Both patients were treated conservatively, and their postoperative course thereafter was uneventful. One patient exhibited severe abdominal pain and all the signs of a duodenal leak, but nothing significant was found on exploration. One patient did have an anastomotic leak but had an uneventful course after drainage. In another patient a subphrenic abscess developed, but without evidence of a leaking duodenal stump. The abscess was drained, and the subsequent course was uneventful.

There were six pulmonary complications. Four, or 16% of the 25, were due to atelectasis, and two were due to pneumonia. This is a surprisingly small proportion, in view of the number of elderly patients in the group. We attribute it to the use of antibiotics, improved anesthetization, early ambulation, and respiratory exercises. One patient had what was thought to be a pulmonary infarct, but no evidence of thrombophlebitis was discovered.

Five complications were directly related to the wound. Two were wound infections, and one was an iodine burn. Two patients had a dehiscence of their wound, which was reclosed with through-and-through silver wire suture. Subsequent recovery was uneventful.

One elderly diabetic patient had a thrombosis of the anterior vertebral artery, and an elderly man had urinary retention postoperatively. The latter problem was controlled by use of an indwelling catheter, and after gastric resection and mobilization the patient was able to void adequately. One patient had thrombophlebitis in a cut-down ankle vein. The cut-down had been made to permit massive blood transfusions, but the complication cleared on treatment with antibiotics.

Of the two fatalities, only one was directly associated with the operative procedure. This patient underwent an emergency operation because of hemorrhage which began again after conservative treatment had been instituted on admission.

At the time of operation there was difficulty in checking the hemorrhage at the base of the ulcer, and several sutures were placed there to stop the bleeding. The patient became icteric postoperatively, and a bile abscess developed. Despite early recognition of this complication and consequent drainage, the course continued to be unfavorable, and death ensued. At autopsy a ligated pancreatic duct and common bile duct, with rupture of the duct at this point, were seen.

The second patient did well postoperatively until the second day, when she complained of weakness in her left arm and inability to flex it. During the third

Fig. 1.—Microscopic section through blood vessel at base of gastric ulcer adjacent to defect, the site of active bleeding (× 62). The patient, a 60-year-old white man (NYH-590-971), was admitted to the hospital because of intractable pain due to undiagnosed metastatic malignant growth. After cervical rhizotomy he did well until the sixth postoperative day, when he vomited large quantities of bright red blood and his blood pressure fell to 90/60. He was treated conservatively for three days but again had a massive hemorrhage. Emergency gastric resection was done. An active, bleeding gastric ulcer was found, and examination of the specimen revealed a defect in a vessel at the base of the ulcer. The patient made an uneventful recovery.

day, while using the bedpan, she suddenly gasped and stopped breathing. Autopsy was limited to the chest and abdomen, and no immediate cause of death was found. It is believed, however, that the patient had a cerebral hemorrhage.

COMMENT

Since the success with surgical treatment for massive hemorrhage from peptic ulcer reported by Finsterer in 1939,[4] there has been a trend away from the ironclad *noli me tangere* attitude. Controversy continues, however, and frequently results in considerable distortion of the problem. A clarification of terms is needed, together with reports on specific methods and their relation to the over-all therapy policy for peptic ulcer. Perhaps a more direct approach may be arrived at if the site of the bleeding is focused upon.

The actual lesion that produces massive hemorrhage from a peptic ulcer is usually an eroded blood vessel, such as is shown in Figures 1 and 2. The photomicrograph and accompanying line sketch are of a bleeding peptic ulcer removed

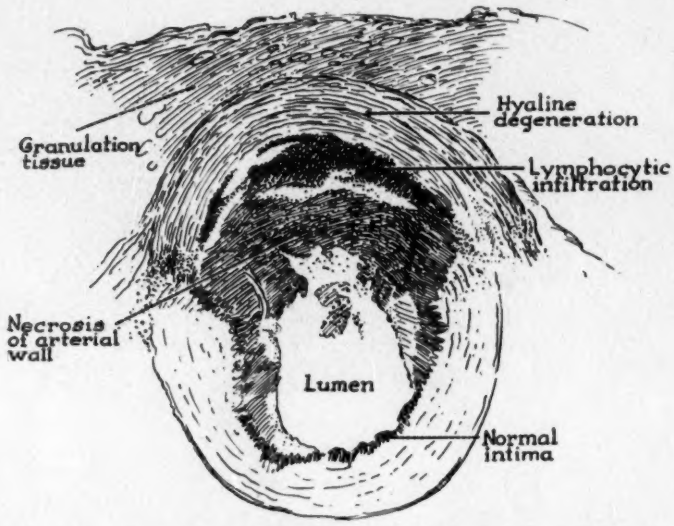

Fig. 2.—Line drawing of Figure 1 demonstrating changes in blood vessel wall.

at operation. Of clinical concern are the factors that determine whether or not bleeding will cease; or, if it has stopped, whether it will begin again. These include the degree of erosion in the vessel wall, the size and depth of the ulcer itself, the amount of scarring, and the structure of the vessel, namely, its ability to contract or the degree of sclerosis present. Added to these factors, and probably equally important, is the degree of digestive activity in the gastric or duodenal contents and the peristaltic activity of these segments. Ways and means to determine these factors accurately in every case are still lacking, although much progress has been made in the past 20 years. With these factors in mind, however, an individual evaluation of each and every patient having massive hemorrhage from a peptic ulcer should provide a sound and practical method of approach.

4. Finsterer, H.: Surgical Treatment of Acute Profuse Gastric Hemorrhages, Surg., Gynec. & Obst. **69**:291-298 (Sept.) 1939.

SUMMARY

Fifty-eight patients with massive hemorrhage from peptic ulcer were treated by subtotal gastric resection during a four-year period, 1946 to 1949. Thirteen patients were operated on as presenting surgical emergencies because of the rapid rate of bleeding that was evident on admission, or because active bleeding continued or began afresh after admission. The remaining 45 patients ceased to bleed on admission or bled little thereafter and were operated on after adequate study and preparation. During this period of four years no patient was lost prior to operation. Two patients died after operation; two had complications for which additional procedures were carried out, and the remaining 54 are now well or have only minimal complaints. The follow-up period for this group is short, however, since it ranges from only one to five years.

The criteria for determining whether or not to operate and when operation should be undertaken on a patient with massive hemorrhage from a peptic ulcer include the following: (1) the rate of bleeding; (2) whether or not the patient has bled before, how frequently and how extensively; (3) his age; (4) his general condition, and (5) his response to conservative management. We believe that, when indicated, gastric resection with removal of the ulcer, if feasible, can be accomplished with less risk to the patient than that associated with conservative management.

END-RESULTS OF REHABILITATION OF WAR WOUNDS OF THE HAND

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OF ALL skeletal mechanisms of the body, that of the hand is not only the most complex but also the most essential to the economic and social independence of the individual. The rehabilitation of hand wounds presents special problems which have become accentuated by the large number of cases produced by warfare. It has been estimated that 6% of the 600,000 persons wounded in the army in World War II received hand wounds.[1] We, therefore, have been interested in examining the end results of a representative sample of this group of 36,000 persons.

Several questions which were not at the time readily answerable frequently arose in the minds of those caring for hand injuries during the early phases after wounding. Some of them were as follows:

1. Should a badly damaged finger be amputated?

2. If amputation is to be done, can the decision be made early and thus save the patient prolonged disability or is it better reserved until a later time?

3. Should plastic reconstructive surgery or physical therapy take priority in a severely damaged hand which needs both?

4. What is the final functional and social result of a given injury destined to be?

We have been unable to find a similar study performed after any war. The reason such studies are not available is, we believe, that a series of wounds of comparable nature is impossible to procure. No two war wounds of the hand are alike. In fact, the degree of damage to bones, tendons, joints, nerves, arteries or muscles in certain cases often cannot be accurately assessed. In the following analysis we have made an attempt to avoid this difficulty which has been at least partially successful. We believe that in any case it presents a useful picture of the past therapy and the present status of a small group of these patients.

This study is part of a program of follow-up studies developed by the Veterans Administration and the National Research Council with the aid of the Army and Navy.

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1. Bunnell, S.: Surgery of the Hand, ed. 2, Philadelphia, J. B. Lippincott Company, 1945, p. 638.

MATERIAL

Selection of Cases.—The Committee on Veterans Medical Problems of the National Research Council procured from the Surgeon General of the Army rosters of all men satisfying one of the following criteria: (*a*) admission to an Army hospital in 1944 with the diagnosis of a laceration wound of the hand or compound fracture involving bones and joints of the carpus or metacarpus; (*b*) admission to an Army hospital in 1944 with loss of part of the hand as the cause of discharge. Those men on the rosters who lived within 100 miles of Boston were identified and numbered 125. The Army clinical records for these men were made available by the Veterans Administration.

We were able to contact and examine 102 of these men all of whom were veterans of World War II, of an average age of 28.5 years, with extremes of 19 and 43 years. The time interval from the date of injury to the date of examination averaged four years and one and a half months, with extremes of two years nine months and five years ten months. Excluded from the study were burns of the hand, fingertip and forearm injuries, and injuries without breaks in the skin, such as simple fractures. Nerve injuries above the wrist were not included unless there was an accompanying wound of the hand.

TABLE 1.—*Causative Agents*

Bullet	46
Shell fragments	41
Land mine fragments	3
Grenade fragments	6
Miscellaneous (parachute line, rope, knife, glass, door crush)	6
Total	102

Causative Agent.—Bullets and shell fragments predominated as causative agents (Table 1). The degree of damage caused by bullets was usually minimal, the functional result depending on whether or not joints were entered (Figs. 1 and 2). That caused by shell or bomb wounds was, however, nearly always severe (Fig. 3).

Principles of Therapy.—All patients were treated originally according to a general plan of therapy initiated by a sterile dressing applied as soon as possible after the wounding in the collecting or clearing station. The next stage in therapy was at the evacuation hospital and consisted of débridement under a tourniquet, with removal of dead tissue and foreign bodies. Although the wounds were in most cases left open, preservation of as much skin as possible was practised with an eye to later closure. In the case of rifle bullet wounds, only the wounds of entrance and exit were excised. Immobilization of fractures in the position of function was undertaken at this time.

Later treatment of the wounds at a general hospital consisted of secondary closure within six days whenever possible. Fractures were further reduced. All precautions against too prolonged immobilization were undertaken, and physical therapy with the emphasis largely on motion of all undamaged parts was immediately instituted. Later reconstruction such as skin and bone grafting was usually postponed until the patient's return to the zone of the interior several weeks later.

These ideal principles of therapy were laid down as objectives. They were followed with varying degrees of success in the patients of this group.

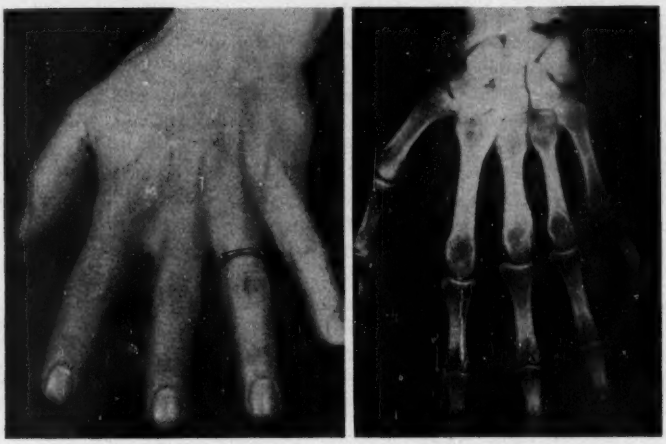

Fig. 1.—Perforating machine-gun bullet wound of hand with minimal damage. The illustration shows the appearance of the hand four years and seven months afterward. The missile entered the dorsum in the region of the second and third metacarpals and left through the palmar aspect of the hypothenar region. There was a fracture of the shaft of the third metacarpal, which can be detected in the roentgenogram only by slight shortening of that bone. Treatment consisted of plaster immobilization for three weeks after local cleaning of the wounds. After two further weeks of active exercises, the patient returned to duty. There was an excellent anatomic functional and economic result.

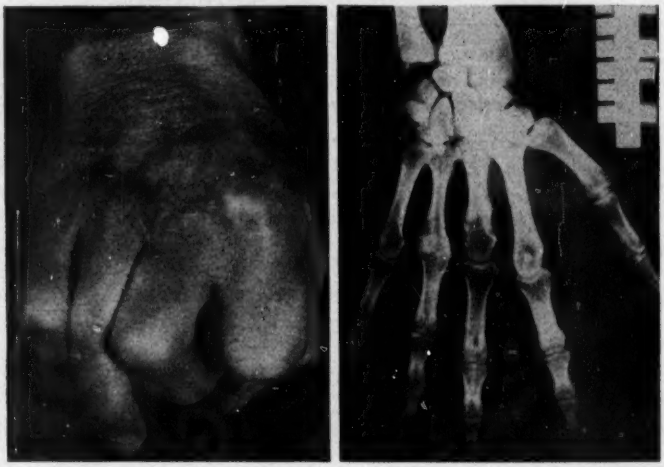

Fig. 2.—Perforating machine-gun bullet wound of hand with moderate damage. The appearance of the hand is shown four years and nine months after wounding. The missile entered the palm and emerged from the dorsum at the level of the third and fourth metacarpophalangeal joints. Treatment consisted of débridement, administration of penicillin, and application of a cast for three weeks. Four weeks after injury a split thickness graft was applied, and seven months later a capsulotomy of the fourth metacarpophalangeal joint was performed. Physical therapy was carried out for one month after injury. The result was good anatomically, fair functionally, and excellent economically. Works full time as a finisher tender.

Method of Analysis.—No precise formula is available for rating the end result of a hand wound. All agree that anatomical deformities are of relatively little importance provided the functional result is good. Economic factors, though important, may be distorted because of lack of incentive. We have, therefore, fallen back on the functional result as evidenced by the patient's ability to perform everyday tasks. Such results must be analyzed either in regard to the functional ability of the hand in question or in regard to that of the individual as a whole. One patient for example, with amputation of one complete hand represents, if considered as a whole, an excellent functional result because of compensation by the use of the opposite hand in doing everyday tasks. Another patient, however, who had a stiff finger in one hand with a normal contralateral hand is worse off, since he had not learned to compensate intelligently. In this study we have, in

Figure 3.—Antipersonnel mine wound of left hand with severe damage. The soldier picked up a booby-trapped can of sardines. The appearance is depicted four years and four months after wounding. The injury caused traumatic amputations of all digits but the fifth and avulsion of skin on both palmar and dorsal aspects. Treatment consisted of débridement and splinting with plaster, two weeks after the injury partial secondary closure, five weeks after injury graft to remaining defect, and five months after injury revision of tip of amputated long finger and flap graft. Physical therapy was used for three weeks after injury. There was a poor anatomic and functional result though an excellent economic result because the patient does not need this hand in his occupation of warehouse manager.

considering the end result of specific therapy, felt compelled to concentrate our attention on the individual injured hand itself.

The results have been rated as excellent, good, fair, poor, and useless. Each is defined as follows:

Excellent—Normal use, strength, motion, coordination and grip, with ability to use the hand for heavy lifting and fine work and for all daily needs, such as eating, dressing, shaving and writing.

Good—Minimal limitation of use. There may be some voluntary guarding because of pain or weakness and slight impairment in doing fine work.

Fair—Moderate limitation. Use of hand limited for daily needs to eating and shaving, with inability to lift heavy objects; grasp of small objects with digits may be present, but hand can be used only as an aid in dressing and writing.

Poor—Marked limitation, loss of strength, grip and ability to hold objects between digits. Hand limited in use for daily needs to functioning as a prop or brace.

Useless—Inability to use the hand at all.

The above categories have been further subdivided into satisfactory results, which include those rated as excellent and good, and unsatisfactory results, which include those rated fair, poor and useless.

GENERAL RESULTS

Sixty-eight per cent of the patients examined showed satisfactory results and 32% unsatisfactory results (Table 2). Lack of mobility of part of the hand was at least partly responsible for the classification "unsatisfactory" in 75.8% of the 33 patients so rated. Pain contributed to the rating in 57.8%. It is of interest that in no case did loss of tissue per se inconvenience the patient. In none of this group was there true causalgia, the pain, when present, being a function of local destruction or deformity.

TABLE 2.—*Functional Results in 102 Patients*

	Excellent	Good	Fair	Poor	Useless	Total	Percentage
Satisfactory results.....	35	34	..	..	..	69	67.65
Unsatisfactory results.....	..	..	27	5	1	33	32.35

The incidence of satisfactory or unsatisfactory results may be affected by the fact that almost 20% of the 125 men failed to report for examination. If, for example, as may well be the case, men with poor results were more likely to cooperate than men with good results, there would be a tendency to find too high a proportion of unsatisfactory results in the men examined. On the other hand, there is no reason to believe that the study of the reasons for poor results will be affected by any possible differences between men who were examined and those who were not.

REASONS FOR POOR RESULTS

In studying the causes of poor results, it has been convenient to subdivide the responsible factors as follows: (1) severity of injury; (2) less than optimal treatment, and (3) the absence of proper rehabilitative drive on the patient's part.

Severity of Injury.—For the purposes of this analysis, the wounds were conveniently divided into two categories, superficial, involving skin and subcutaneous tissue only, and deep, involving bone, tendon, nerves and muscle. Sixteen patients had superficial and 86 deep wounds. Of the 33 patients with unsatisfactory results, all suffered deep wounds. However, 53, or 75%, of the patients with satisfactory results also had deep wounds, many of them of a severity equal to those of the unsatisfactory group (Table 3). It is obvious that the severity of the injury is a most important factor determining the end result.

Less Than Optimum Treatment.—Nearly as significant as the factor of severity was that of the unavailability of optimum treatment. Since the wounds studied were incurred in combat, optimum treatment was not continuously available in all cases because of the exigencies of the situation. It was feasible from studying the records to separate the patients into two categories on this score, 67 of whom had had optimum treatment and 35 of whom had not. It was striking to note that 28 of the 33 patients with unsatisfactory results, or 85%, had had less than optimum treatment, whereas this was true in only 7, or 10.1%, of those with satisfactory results.

Lack of Rehabilitative Drive.—This was a factor which is difficult to measure accurately. The figures cited in Table 3 are the result of a prolonged interview designed to assess the patient's ability to make a maximum effort toward an optimal result. Of the 102 patients studied, 16 were considered to have inadequate rehabilitative drive. Only five of these patients fell in the group of 69 who had satisfactory results, whereas 11, or one-third, of the 33 patients with unsatisfactory results were considered to have inadequate rehabilitative drive.

TABLE 3.—*Causes of Poor Results*

	Deep Wounds	Less Than Optimal Treatment	Poor Rehabilitative Drive
Thirty-three unsatisfactory results	33 (100%)	28 (84.9%)	11 (33.3%)
Sixty-nine satisfactory results	53 (76.8%)	7 (10.1%)	4 (5.7%)

SPECIFIC FORMS OF THERAPY

Amputation of Digits.—Only an indirect answer can be given to the question as to whether a severely damaged finger is better preserved or amputated. Of the 102 patients, 41 complained of stiff fingers. In 25 instances this lack of mobility contributed to or was the principal cause of the unsatisfactory result. At the follow-up examination it was the opinion of the examiner that 10 of the patients would be benefited by amputation of one or more digits. Five of these 10 actually asked for it. The conclusion is that amputation of a severely damaged finger should be performed provided other mobile fingers remain to perform the grasping function. If no other mobile fingers remain, the hand can then be used only as a hook, a prop, or a brace for which the stiff finger, provided it is painless, should be preserved.

Table 4 presents data which have been accumulated on the question of whether amputation should be done early or late. It can be seen that although the incidence of unsatisfactory results was slightly greater in the patients in whom amputation was done early than in those in whom it was done late, the difference was insignificant. The length of hospitalization after wounding can, however, be seen to be greatly different in the two groups, with the early amputation group showing a much shorter duration. The evidence presented tends to indicate that once it becomes apparent that a damaged finger will be stiff it should be amputated provided there is other mobile tissue to preserve the grasp. Although from the point

of view of the end result it is not harmful to postpone this maneuver it is economically and psychologically more sound to perform it early rather than late. An interesting psychological aspect was brought out by the remark of one patient with a stiff finger contributing to an unsatisfactory result, who, when it was suggested at the time of examination that he have the finger removed, stated "I was hoping that they would do that in the beginning, but the doctors spent so much time and effort in preserving it that now I would not feel right about having it amputated."

Obviously the issues raised here cannot be entirely settled by the evidence at hand. One might argue that some of the satisfactory results with stiff fingers make a case for the postponement of digital amputation or the complete abandonment thereof. In none of those patients, however, was there evidence that amputation of the stiff finger would have been harmful. In many, in fact, it appeared that the end result might have been made even better.

TABLE 4.—*Amputations*

Type of Amputation	Total Number of Patients	Unsatisfactory Results	Average Days Hospitalized	Average Days Disabled
Early	17	41.2%	235.8	291.8
Late	12	33.3%	405.8	576.5

TABLE 5.—*Effects of Less Than Optimal Physical Therapy in 27 Patients with Fractured Metacarpal*

	Number of Patients	Result	
		Satisfactory	Unsatisfactory
Patients with less than optimal physical therapy	7	0	7
Patients with adequate physical therapy	20	20	0

Physical Therapy.—A patient was considered to have had adequate physical therapy if he received supervised active motion to the injured hand starting as soon as was consistent with the healing of the wound and continuing daily for a minimum of three months. Our study showed that all the patients who were treated with less than optimum physical therapy achieved unsatisfactory results (Table 5). Looking at it another way, of the 33 patients with unsatisfactory results, 26, or 78.8%, had less than optimum physical therapy. This was also true in 37, or 88.1%, of the 42 patients who showed stiff fingers.

Frequently the reason for the fact that an individual patient received less than optimum physical therapy was beyond control. The hands of 15 patients, for example, were purposely immobilized longer than desirable from the point of view of ideal physical therapy because it was felt that in their cases skin grafting and the immobilization of fractures took greater priority. Eleven of them are left with stiff fingers. It is difficult merely from studying the army records to determine whether in any individual patient the decision which was made in this regard was wrong. Early active motion, however, appears to be the most important factor in proper therapy of hand wounds.

MISCELLANEOUS CONSIDERATIONS

Unemployment.—Only four of the 102 patients were unemployed at the time of the follow-up examination. Only one of these four patients had an unsatisfactory functional result according to the criteria discussed. It therefore seems likely that their unemployment was the result of factors other than the hand wound. The low incidence of unemployment is a reflection of the excellent vocational rehabilitation afforded the patients by the government.

Pensions.—Ninety-three of the 102 patients were receiving pensions which varied in amount from 10 to 70% of the maximum allowed for a patient who is totally disabled.

Type of Work.—The types of occupation are listed (Table 6). They are divided into three categories: those occupations in which the loss of use of one hand is not necessarily important, those in which light use of one hand and full

TABLE 6.—*Employment Status*

1. No use of one hand permissible			29
	Inspector	Shipper	
	Lawyer	Student	
	Meter Reader	Supervisor	
	Salesman	Tax collector	
	Unemployed (4)		
2. Light use of one hand permissible			42
	Clerk	Packer	
	Grocer	Photographer	
	Machine operator	Printer	
	Mail carrier	Repairman	
	Truck Driver		
3. Full use of both hands required			31
	Baker	Electrician	
	Baler	Laborer	
	Construction work	Mechanic	
	Mill worker		

use of the other is presumably necessary, and those in which full use of both hands is necesasry. The patients fell roughly in equal numbers into each category. When analyzed from another angle it was discovered that 39 patients were able to carry out the same work as they had performed before wounding whereas 63 were engaged in lighter occupations. Here again the Department of Vocational Rehabilitation had performed a great service.

Self-Inflicted Wounds.—The problem of the self-inflicted wound has always been a minor but disturbing one in the armed forces. The characteristic self-inflicted wound involved, in former years, the trigger finger.[2] For some reason which we have been unable to analyze, it has more recently been an injury of the palm of the left hand, usually through the fourth metacarpal.[1] Although in seven instances the wounds were inflicted by the patient's own weapon and in five of them the left hand was injured, the records betray no suspicion of self-infliction at the time of original observation.

2. Hart, A. G.: The Surgeon and the Hospital in the Civil War, in Papers of the Military Historical Society of Massachusetts, 1902, Vol. 13, p. 265.

Foreign Bodies.—The presence of retained foreign bodies has various implications which are at least partly psychological.[3] There was a high incidence of patients with retained foreign bodies, namely 32, or 31.3%, of 102. Thirty-one of them were completely asymptomatic. Eight had a single foreign body, and 24 had multiple foreign bodies. There seemed to be no connection between foreign bodies and pension neurosis, as has been noted in other studies.

SUMMARY

A follow-up study of 102 patients with severe war wounds of the hand has revealed that favorable results are proportional to the lack of severity of the injury, the adequacy of therapy, and the patient's rehabilitative drive.

The great importance of adequate physical therapy is emphasized. The importance of stiff fingers as the chief cause of poor end results and the desirability of early amputation thereof are brought out. When there is a conflict of priorities between early active motion and reconstructive surgery which requires prolonged immobilization, the former should take priority.

The employment status of the group studied was favorable, only 4, or 3.9%, of the men being unemployed.

3. Botsford, T. W., and Freni, D. R.: Late Reactions to Metallic Foreign Bodies, New England J. Med. **238**:385-390 (March) 1948.

ARNOLD-CHIARI MALFORMATION

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THE CLINICAL importance of developmental anomalies and malformations of the cervicomedullary juncture is being increasingly appreciated in neurological and neurosurgical centers. The most frequent of these processes is the Arnold-Chiari malformation (caudal displacement of brain stem, cerebellum, and spinal cord), as the fairly considerable number of articles on this subject in the recent literature will attest.

Nevertheless, there are still great disagreement on the pathogenesis of the Arnold-Chiari malformation and little concurrence on the relation of platybasia and spina bifida. Discussion continues on the role of this process in the hydrocephalus of infants with spina bifida. The historical data, the findings on examination, or roentgenographic evidence which should suggest the diagnosis in the adult patient, and the methods for elucidating the proof of diagnosis, remain poorly delineated. In surgical therapy results have been variable, but here at least the majority of writers (though by no means all) have eventually agreed upon an operative regimen which has been recognized as giving a high percentage of successful results.

During the past three years three adult patients with the Arnold-Chiari syndrome have been seen at the Mount Sinai Hospital. In all three the diagnosis was suggested correctly and was then preoperatively well demonstrated. All three had successful surgical intervention.

It is felt that many of the disputed questions arising in the study of such patients can be satisfactorily answered from the combination of our limited material and the correlation of the fairly extensive literature.

REPORT OF CASES

CASE 1.—C. L., a 25-year-old white married man who did clerical work, was admitted to Mount Sinai Hospital in Oct. 1947. For several years he had noted occasional headaches, rather generalized in distribution. These headaches were present on awakening and were associated with stiffness of the neck. However, improvement of the headache occurred on recumbency. He had slight difficulty in walking in the dark at this time.

There was no apparent progression until March, 1947, when left supraorbital headaches became fairly constant and there was an associated sensation of tightness at the base of the skull posteriorly. At the same time he began to notice weakness and tiredness of both legs. There were slight progression of the weakness and some further unsteadiness of gait, with a

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sensation of falling forward when going down steps. Visual difficulty, described as blurring on looking at moving objects which was not present when looking at fixed objects, progressed slowly from March, 1947. At the same time rapid change in direction of gaze precipitated vertigo.

The past history contributed the statement that in 1937 there was limping of the right leg. At that time it is said that a physician found some numbness of the lateral surface of the right leg and some muscle weakness but made a diagnosis of anterior poliomyelitis. The patient recovered spontaneously from this illness within three months.

The general physical examination was noteworthy because of the presence of bilateral pes cavus. A small tuft of hair was present over the lower dorsal vertebrae.

Neurological studies revealed the patient to be well adjusted and mentally normal. He had a wide-based gait, somewhat spastic and unsteady, with a tendency to veer to the right. There was decreased arm swing on the left. In the Romberg position the patient swayed with his eyes open and fell to the right with his eyes closed. Slight finger-to-nose ataxia on the left and slight dysdiadochokinesis, more on the left than on the right, were present.

No motor loss was demonstrable. There was increased tonus of both extremities, and the tendon reflexes were hyperactive but equal. Plantar responses were extensor, bilaterally. The abdominal and cremasteric reflexes were unobtainable. There was a slight diminution of vibration sense in the lower extremities, more definite on the right. Position sense was also decreased on the right, though only slightly. Other sensory modalities were normal.

Funduscopic examination revealed the disks filled and the margins indistinct, with an appearance suggestive of glial streaking extending over the disk margins. The veins were full and dark, and the arteries were normal. The extraocular movements were normal, but there was a horizontal nystagmus, with sustained rapid and fine movements to the right and sustained, but coarse, movements to the left. There was vertical nystagmus on upward gaze. The corneal reflexes were depressed bilaterally. Flattening of the left nasolabial fold and a hyperactive jaw jerk reflex were noted. The gag reflexes were hypoactive. The remainder of the cranial nerves were normal. Audiometric tests had normal results. Caloric stimulation was able to produce nystagmus in the proper direction, with stimulation of both horizontal and vertical canals, but no past pointing, vertigo, or nausea could be elicited.

An electroencephalogram revealed a large amount of diffuse and symmetrical 4-to-6-per-second activity without focal accentuation. This was interpreted as being consistent with a moderate degree of diffuse cerebral dysfunction, the cause of which could not be determined from the tracing.

A lumbar puncture was done. The initial pressure was 160 mm. of water, which fell to 70 mm. after removal of 15 cc. of clear colorless cell-free fluid. The total protein was 100 mg. per 100 cc.

Roentgenograms of the skull revealed increased convolutional markings and were, to a certain extent, suggestive of some of the features of basilar impression (Fig. 1). Roentgenograms of the cervical portion of the spine showed fusion of the second and third cervical vertebral bodies. Thoracic films disclosed spinal fusion of the bodies of the sixth, seventh, and eighth thoracic vertebrae and distortion of their posterior arches, with intact pedicles. The lumbar portion of the spine showed anomalies of failure of fusion of the posterior arches of the lower lumbar bodies.

The diagnosis of Arnold-Chiari malformation was considered, justified on the basis of the clinical picture and the roentgenologic findings. It was believed that myelography with ethyl iodophenylundecylate (pantopaque®) would be most instructive in delineating the lesion. Ethyl-iodophenylundecylate was injected through the lumbar route. With the patient inverted, a partial obstruction at the second cervical vertebra was demonstrated (Fig. 2). The upper end of the column extended one vertebra cephalad on the left side. The opaque medium was seen to drip through the foramen magnum slowly on the left side only. There was free flow without distortion throughout the lumbar and dorsal regions.

Accordingly, low suboccipital craniotomy and cervical laminectomy were done by one of us (I. C.) on Oct. 30, 1947 (Fig. 3). There was a peculiar asymmetry of the occipital bone. There was a failure of fusion of the atlas, so that a space of at least 1 cm. was present between the ends of the arch. No other abnormality was noted. Occipital bone was removed to uncover

Fig. 1.—Roentgenogram of right lateral portion of skull film in Case 1, demonstrating high position of odontoid process, moderate flattening of basal angle, and fusion of first and second cervical vertebrae.

Fig. 2.—Myelogram (ethyl iodophenylundecylate) in Case 1. Film taken with patient tilted head down at 85 degrees but with head in moderate extension. Oil is blocked at third cervical vertebra with concave upper border.

an area of dura approximately 5 cm. in diameter, including the posterior rim of the foramen magnum. Part of the arch of the atlas and the spines and laminas of the second cervical vertebra and subsequently of the third were removed. The dura over the cerebellum was opened in a V-shaped manner, the point of the V being at the foramen magnum. From this point on, the cervical dura was opened by a straight midline incision. There was immediately noted an elongation of the cerebellar tonsils, which extended from the foramen magnum down to the third cervical vertebra. When the tonsils were separated, the normal-appearing floor of the fourth ventricle was brought into view. An arachnoid band was present at the site of the foramen magnum. This band compressed the tonsils. There was another thickened arachnoid adhesion which bound the spinal cord on the right side to the posterior arachnoid just at the tip

Fig. 3.—Operative photograph in Case 1. The cerebellar tongues extend down to third cervical vertebra (level of lowest dural-traction suture).

of the right tonsil. When this was freed, there was a gush of spinal fluid from below, even though the patient was in the sitting position. No attempt was made to free the tonsils or to resect them. When the cord was pulled to either side, cervical roots were exposed, running cephalad from the cord to their foramens of exit. The dura was left wide open. Over the exposed cervical cord and tonsils were placed thin sheets of absorbable gelatin sponge (gelfoam®) wet in saline solution. Considerable time was spent securing hemostasis, and a layer closure of the wound was carried out.

Postoperatively the patient's course was uneventful. Relief of the headache and vertigo, clearing of the visual difficulty, and return of a relatively normal gait were noted. The neurological examination at the time of discharge (three weeks postoperatively) showed only a

minimal unsteadiness of gait, with persistence of the horizontal nystagmus but disappearance of the vertical. The Babinski sign was still present on the left but the right plantar response was now flexor. There were minimal dysdiadochokinesis and slight tremor of the outstretched hands.

When the patient was last examined in April, 1950, the only residual finding was slight horizontal nystagmus. The patient was asymptomatic.

Case 2.—M. L., a 32-year-old single woman, a kyphoscoliotic dwarf, was admitted to the Mount Sinai Hospital in August, 1949, complaining of difficulty in walking and paresthesias of all extremities. For five years prior to admission, sneezing produced occipital pain radiating into both shoulders and a residual throbbing occipital headache.

Fig. 4.—Roentgenogram of lumbodorsal portion of spine in Case 2. Taken on a single 14 by 17 in. plate (35.6 by 43 cm.), it demonstrates the deformity in this kyphoscoliotic dwarf.

More recently, sneezing precipitated loss of balance, obliging her to find support to prevent falling. Tingling and numbness began in the left foot one year prior to admission and extended gradually to involve the other extremities. Her sense of touch was impaired, and she experienced difficulty in sewing and other fine activities requiring the use of her hands. Other symptoms included progressive difficulty in walking, blurring of vision, and diplopia. The last was aggravated by sudden movements of the head.

Physical examination disclosed a poorly developed woman only 4 ft. 5 in. (134.6 cm.) tall, weighing 78 lb. (35.4 kg.). She presented numerous stigmata of congenital defects, including a high-arched palate, peculiar shape of several fingers and toes, several vascular nevi, numerous

café-au-lait spots, and marked kyphoscoliosis. Her gait was ataxic, with a tendency to veer to the left. Some fibrillary twitching of the tongue was evident. Horizontal nystagmus was elicited, with coarse movements to the left and fine and well-sustained movements to the right. The cranial nerves were otherwise normal. Dysdiadochokinesis and heel-to-knee ataxia were present on the left; the only right cerebellar signs were minimal dysmetria and terminal decomposition on the finger-to-nose test. Tendon reflexes were generally hyperactive

Fig. 5.—Cervical myelogram (ethyl iodophenylundecylate) in Case 2. Film taken with patient tilted head down at 60 degrees, with head in flexion. Defect in the column of ethyl iodophenylundecylate shows extension of cerebellar tissue down to second cervical vertebra. Small amount of oil has entered foramen magnum and outlines the basilar artery.

and abdominal reflexes absent. Bilateral Hoffmann signs and a Babinski sign on the right were found.

Lumbar puncture with the Queckenstedt test revealed a partial block in the vertebral canal, and the spinal fluid protein was elevated to 79 mg. per 100 cc.

Roentgenographic examination of the spine (Fig. 4) demonstrated pronounced rotatory kyphoscoliosis in the dorsal region. There was no evidence of spinal anomaly. A skull roent-

genogram showed increased convolutional markings, flattening of the basal angle, and elevation of the odontoid process into the foramen magnum, compatible with a diagnosis of slight basilar impression.

The diagnosis of probable Arnold-Chiari malformation was made, and it was decided to do a study with ethyl iodophenylundecylate. Oil injection into the lumbar region demonstrated no lumbar or thoracic abnormality, other than the kyphoscoliosis. Cervical examination demon-

Fig. 6.—Operative photograph in Case 2. Extension of cerebellar tissue down to second cervical vertebra is clear. Between the cerebellar tissue and the spinal cord, the "medullary nodule" is seen.

strated the presence of a typical tongue-like mass extending down from the foramen magnum to the middle of the second cervical segment (Fig. 5). Through small lateral channels the oil extended upward along the clivus, where it outlined the basilar artery but demonstrated no other posterior-fossa abnormality. The diagnosis of Arnold-Chiari malformation was considered confirmed, and operation was advised.

On Aug. 25, 1949, one of us (S. W. G.) performed suboccipital craniectomy and cervical laminectomy of the first, second, and third cervical laminas. No bone abnormality was noted.

The dura was opened as a V-shaped flap with the apex at the foramen magnum, and a midline incision extended downward. The elongation of the cerebellar tonsils extended from the foramen magnum to the middle of the second cervical lamina. Caudad to the tonsils was a rounded protuberance, apparently a so-called medullary nodule (Fig. 6).

No attempt was made to free or otherwise interfere with the tonsils. Gentle retraction of the cord to the right and the left revealed a cephalad course of the first and second cervical roots. Adequate bone and dural decompression was afforded, and the usual layer closure was done.

The postoperative course was uneventful, and the patient was discharged three weeks later. At this time slight regression of symptoms was noted, but there was little change in her neurological signs. Follow-up studies over a one-year period have shown a slow but steady regression of her symptoms. The headache, neck pain, and visual disturbances have disappeared completely. The numbness and tingling have almost entirely gone, and the gait has improved, though it is still somewhat ataxic. The nystagmus, diminished corneal reflexes, and pyramidal tract signs are unchanged, but the cerebellar function has returned nearly to normal.

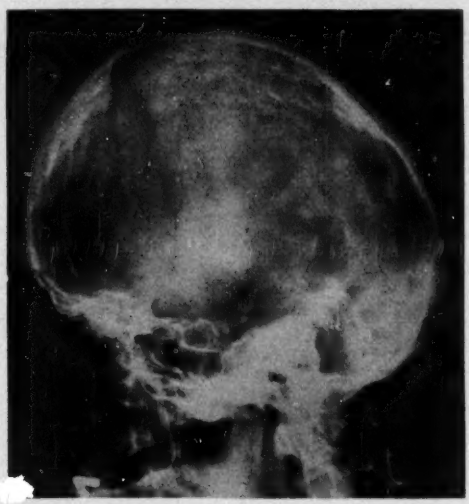

Fig. 7.—Roentgenogram of right lateral portion of skull in Case 3, showing the moderate oxycephaly, high odontoid process, and flat basal angle.

CASE 3.—I. Z., a 39-year-old man who for many years had been considered a victim of multiple sclerosis, was admitted to the Mount Sinai Hospital for reevaluation of his condition on Dec. 14, 1949.

He had a history of mild difficulty in urination for 14 years and an eight-year history of difficulty in walking and stiffness of the extremities. He had been sexually impotent for several years. For two years there had been progressive loss of hearing and numbness in the fingers and hands. There was a suggestion of partial remissions.

The patient was a tall, well-developed man, with a peculiarly shaped, somewhat steeple-shaped head. There was a markedly spastic gait, requiring use of canes for any walking. Spasticity and slight weakness involved all extremities, the right more than the left. There were hyperactive deep reflexes and bilateral Babinski signs, with absence of abdominal and cremasteric reflexes. He had a serious nerve-type hearing impairment bilaterally, audiometrically demonstrated to be severest for higher tones, but averaging 30 db. The remainder of the cranial nerves were normal.

A lumbar puncture yielded clear fluid, with normal hydrodynamic pressure and a protein content of 43 mg. per 100 cc. Skull roentgenograms were at this time interpreted as showing only a mild degree of oxycephalic change. Complete spinal films were normal. A cervical myelogram was performed, with visualization by ethyl iodophenylundecylate by lumbar injection. The highest level examined was the third cervical vertebra, and this study was considered as showing no abnormality. The patient was discharged from the hospital on Jan. 1, 1950, with the diagnosis of probable multiple sclerosis continued.

Fig. 8.—Cervical myelogram in Case 3. Film taken with patient tilted head down at 60 degrees with the head in moderate flexion. Oil is obstructed at the upper border of second cervical vertebra by a bilobar mass. Small amount of oil has entered foramen magnum and lies against the clivus, outlining the basilar artery.

The roentgen studies were reviewed shortly after the patient was discharged. The skull appeared definitely steeple shaped, with increased convolutional markings. The basal angle was quite flat, measuring 164 degrees. The line of the hard palate, if extended to the posterior rim of the foramen magnum (Chamberlain's line), crossed the odontoid process 1.5 cm. from its apex. The odontoid process extended into the anterior portion of the foramen magnum

(Fig. 7). The diagnosis of marked basilar impression was made, and the patient was asked to return to the hospital for reinvestigation of the foramen magnum region.

He was readmitted to the Mount Sinai Hospital on Jan. 16, 1950. There had been no change in the clinical picture. On Jan. 19 another myelogram was done by lumbar injection of ethyl iodophenylundecylate. No abnormality was demonstrated in the lumbar or thoracic canal. As the oil was passed into the foramen magnum region, it demonstrated a bilobed defect, separated by an incisura, extending down from the foramen magnum to the lower edge of the arch of the atlas (Fig. 8). The oil could be passed by this defect laterally and then was allowed to flow up the clivus to the base of the posterior clinoid processes, outlining a normal

Fig. 9.—Operative photograph in Case 3. Cerebellar tonsils extend to upper border of second cervical vertebra and were constricted by foramen magnum. A dense adhesion corresponds to site of resected arch of atlas. Photograph was angled laterally to show normal course of upper cervical nerves.

configuration of the vertebral and basilar arteries. At the conclusion of the examination all the oil was returned to the lumbar sac and removed. It was concluded that definite caudal displacement and herniation of the cerebellar tonsils were present. Decompression of the abnormality was decided upon.

On Jan. 24, one of us (L. M.) performed bilateral suboccipital craniectomy and upper cervical laminectomy, through a midline vertical incision. The dura was opened in a Y-shaped manner to expose the cerebellum, cerebellar tonsils, and upper cervical cord (Fig. 9).

The thick and heavy cerebellar tonsils extended down through the site of the unroofed foramen magnum to reach the lower border of the arch of the atlas. A thick, adhesive band crossed the lower portion of the tonsillar herniation. The first and second cervical nerves retained their caudad course, not having the cephalad course usually described in the Arnold-Chiari malformation. There was no evidence that displacement of the brain stem had occurred. The tonsils and their adhesions were not disturbed. The usual layer closure of the wound was performed over a wide dural decompression. A final diagnosis of Arnold's deformity of the cerebellum was made, in contradistinction to the combined Arnold-Chiari malformation. He was retained in the hospital until March 24, to permit rehabilitative physical therapy. At the time of discharge he had increased motor power, with decreased spasticity, so that he was able to walk without a cane. The hearing had improved to the point where impairment was no longer clinically obvious. The urinary difficulty had completely disappeared. Though his reflexes were still hyperactive, the plantar responses were no longer extensor.

When last examined in May, 1950, he volunteered the further information that he had regained sexual potency, and his improvement generally continued.

In this patient no spinal vertebral abnormality could be demonstrated, and there was no evidence of medullary displacement to accompany the cerebellar herniation. However, as will be discussed later, in 14 of Chairi's original 21 cases only tonsillar displacement, without appreciable displacement of the medulla, was demonstrated, and among all 14 anatomically studied cases only one instance of spina bifida was demonstrated.

COMMENT

In 1891 Chiari [1] described a child with hydrocephalus in whom there was displacement of the fourth ventricle to the level of the fifth cervical vertebra. However, the maldevelopment of the cerebellum and the medulla associated with hydrocephalus and spina bifida was first described by Arnold [2] in 1894, and in the following year it was described independently by Chiari [3] with a series of 21 cases.

Schwalbe and Gredig [4] in 1907 described very completely the findings of careful morphological studies of four cases and suggested the designation of the lesion as the Arnold-Chiari malformation.

Apparently, the entire subject of the malformation was forgotten or neglected, except for a few pathologic studies in the German literature, until in 1932 van Howveninge Graftijk [5] described his first operative attempts at treatment of this deformity. All his patients died of complications of the operative procedures.

In 1935 Russell and Donald [6] redirected the attention of neurologists and neurosurgeons to the entire subject with a scholarly review of 10 patients who had myelomeningocele, each of whom was shown at autopsy to have the Arnold-Chiari

1. Chiari, H.: Über Veränderungen des Kleinhirns in Folge von Hydrocephalie des Grosshirns, Deutsche med. Wchnschr. **17**:1172-1175, 1891.

2. Arnold, J.: Myelocyste, Transposition von Gewebskeimen und Sympodie, Beitr. path. Anat. **16**:1-28, 1894.

3. Chiari, H.: Über Veränderungen des Kleinhirns, des Pons und der Medulla oblongata in Folge von congenitaler Hydrocephalie des Grosshirns, Denkschr. k. Akad. Wissensch. Math-naturw. Kl. **63**:71-116, 1895.

4. Schwalbe, E., and Gredig, M.: Über Entwicklungsstörungen des Kleinhirns, Hirnstamms und Halsmarks bei Spina bifida: Arnold'sche und Chiari'sche Missbildung, Beitr. path. Anat. **40**:132-194, 1907.

5. van Howveninge Graftiik, C. J.: Over Hydrocephalus, Doctorate Thesis, Leyden, Netherlands, Edwardo Ijdo, 1932; cited by Russell, D. S., and Donald, C.: The Mechanism of Internal Hydrocephalus in Spina Bifida, Brain **58**:203-215, 1935.

6. Russell, D. S., and Donald, C.: The Mechanism of Internal Hydrocephalus in Spina Bifida, Brain **58**:203-215, 1935.

malformation. This was the first mention of the condition in the English language. Russell and Donald suggested the possibility of surgical therapy, but none of their patients were treated surgically.

Aring,[7] as well as Penfield and Coburn,[8] in 1938 reported unsuccessful attempts at surgical correction. The first successfully treated patient was operated upon May 18, 1936, and was reported on by McConnell and Parker [9] in 1938.

MORPHOLOGIC ASPECTS AND PATHOGENESIS

Morphologically little has been added to the original work of Arnold,[2] Chiari,[10] Sträussler,[11] and Schwalbe and Gredig.[4] The malformation consists essentially of a cerebellar abnormality in which the obvious feature is the presence of two tongue-like extensions of abnormal cerebellar tissue along the dorsal surface of the cervical neuraxis. These prolongations are usually referred to as the cerebellar tonsils, though they may not be homologous. The cerebellum is grossly abnormal, and no vermis is present, as shown by Russell and Donald [6] and recently noted by Chorobski and Stepién.[12]

It is possible for the cerebellar abnormality to exist with little displacement of the medulla oblongata, this situation being termed the Arnold deformity. More frequently, the medulla lies anterior to the malpositioned tongues of cerebellar tissue and, thus, is largely caudad to the foramen magnum. The shift of the medulla is the Chiari malformation. Any degree of chronic arachnoid adhesions may form here, perhaps blocking the foramens of Luschka or Magendie or producing a perimedullary subarachnoid block.

The displaced structures are subject to vascular impairment, perhaps with cystic degeneration; other forms of cystic change may occur, as in rupture and dilation of the central canal due to obstruction of the fourth ventricle. The relationship to syrinx formation has been discussed by Lichtenstein.[13]

The so-called medullary nodule is frequently described as lying just caudal to the extension of the cerebellar tongues. This "nodule" apparently represents an overfolding of the dorsal medulla at the cervicomedullary junction. The fourth ventricle is, of course, within the nodule, and, if the "cystic area" below the cerebellar tonsils is subjected to needle aspiration, fourth-ventricle cerebrospinal fluid is obtained.

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7. Aring, C. D.: Cerebellar Syndrome in an Adult with Malformation of the Cerebellum and Brain Stem (Arnold-Chiari Deformity), with a Note on the Occurrence of "Torpedoes" in the Cerebellum, J. Neurol. & Psychiat. **1**:100-109, 1938.

8. Penfield, W., and Coburn, D. F.: Arnold-Chiari Malformation and Its Operative Treatment, Arch. Neurol. & Psychiat. **40**:328-336 (Aug.) 1938.

9. McConnell, A. A., and Parker, H. L.: A Deformity of the Hindbrain Associated with Internal Hydrocephalus: Its Relation to the Arnold-Chiari Malformation, Brain **61**:415-429, 1938.

10. Chiari.[1,3]

11. Sträussler, E.: Über eine eigenartige Missbildung des Zentralnervensystems, Jahrb. Psychiat. u. Neurol. **25**:1-56, 1905.

12. Chorobski, J., and Stepién, L.: On the Syndrome of Arnold-Chiari: Report of a Case, J. Neurosurg. **5**:495-500, 1948.

13. Lichtenstein, B. W.: Distant Neuroanatomic Complications of Spina Bifida (Spinal Dysraphism), Arch. Neurol. & Psychiat. **47**:195-214 (Feb.) 1942; Cervical Syringomyelia and Syringomyelia-like States Associated with Arnold-Chiari Deformity and Platybasia, ibid. **49**:881-894 (June) 1943.

The frequently mentioned upward inclination of the intrathecal course of the cervical nerve roots is the obvious result of caudal displacement of the cervical portion of the spinal cord. The lower cranial nerves are then even more greatly distorted because of the greater caudad displacement of the brain stem.

Opinion remains divided regarding the pathogenesis of the condition. The traction mechanism, in which the cerebellum and medulla are presumably displaced as a result of fixation of the cord in the myelocele sac, is a suggestive concept. However, it fails to explain the existence in some cases of cerebellar displacement without medullary displacement. To explain the overfolding of the medulla and cervical cord to produce the so-called medullary nodule by the traction mechanism renders the reasoning cumbersome and implausible. In addition, the presence of conditions as originally reported by Chiari [3] and as described in Bucy and Lichtenstein's patient,[14] in whom no spinal anomaly of fixing type was demonstrable, and in Sträussler's patient,[11] in whom cerebellar tissue extended to the lumbar sac, militates against this explanation.

In Penfield and Coburn's [8] case the traction force was apparently demonstrated at the operating table; that is, when freed of adhesions, the cerebellar tongues immediately retracted up into the foramen magnum. We suggest that the retraction in such a circumstance may well have been the result of the marked forward flexion of the head used for the operative exposure. Hurteau [15] has noted the effect of head position on the position of the tonsils. It is easy enough to conceive of traction by cord fixation leading to a gradual stretching and readjustment of tissue positions, with an eventual permanent malposition, but to conceive of a long-standing traction force with the neuraxis reacting to this force much like a rubber band is to ignore the physical properties of the tissue.

Several authors have warned against resection of tonsillar tissue (Penfield and Coburn,[8] McConnell and Parker,[9] Adams, Schatzki, and Scoville,[16] and Ogryzlo [17]), on the basis that such resection permitted the entire traction force to be exerted through the medulla and thus led to damage of vital areas. It seems more likely that such tonsillar removal is prone to damage the medulla both directly as a result of operative manipulation and indirectly by interference with the vascular supply. In two recently reported cases, one by Swanson and Fincher [18] and the other by Lewin, Wycis, and Young,[19] successful surgical results were obtained with complete tonsillar resection.

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14. Bucy, P. C., and Lichtenstein, B. W.: Arnold-Chiari Deformity in an Adult Without Obvious Cause, J. Neurosurg. **2**:245-250, 1945.

15. Hurteau, E. F.: Arnold-Chiari Malformation, J. Neurosurg. **7**:282-284, 1950.

16. Adams, R. D.; Schatzki, R., and Scoville, W. B.: The Arnold-Chiari Malformation: Diagnosis, Demonstration by Intraspinal Lipiodol and Successful Surgical Treatment, New England J. Med. **225**:125-131, 1941.

17. Ogryzlo, M. A.: The Arnold-Chiari Malformations, Arch. Neurol. & Psychiat. **48**:30-46 (July) 1942.

18. Swanson, H. S., and Fincher, E. F.: Arnold-Chiari Deformity Without Bony Anomalies, J. Neurosurg. **6**:314-319, 1949.

19. Lewin, J. R.: Wycis, H. T., and Young, B. R.: Roentgen Diagnosis of Herniation of the Brain into the Spinal Canal (Arnold-Chiari Deformity) by Pantopaque Myelography, Radiology **54**:591-594, 1950.

Gardner's [20] concept was that the malformation is merely a result of chronic hydrocephalus and, thus, really a form of chronic pressure cone in certain patients whose neoplasms cause slowly increasing intracranial pressure. However, certain differences must be pointed out: The Arnold-Chiari malformation may occur in the presence of normal intracranial pressure, with ventricles of normal size, as in the cases of Aring,[7] Ogryzlo,[17] and Hurteau.[15] In addition, the absence of a cerebellar vermis and true tonsillar tissue cannot be explained except as a primary malformation.

As List [21] so clearly pointed out, these structural changes suggest that this condition is primarily a maldevelopment of the hindbrain, at a point where the medullary folds close to form the medullary tube. The teratogenic point of determination of the deformity, therefore, may coincide with the time of closure of the medullary tube or a slightly later period, which corresponds to the teratogenic time for production of a spina bifida and myelomeningocele.

In our own belief that the malformation is, therefore, a primary change, we recognize, of course, that the presence of such a process will indeed frequently produce hydrocephalus, which will then increase the deformity. In addition, a low cord fixation could tend to increase the displacement by requiring the neuraxis to assume an unusually great length.

CLINICAL FEATURES

Forty adult and adolescent patients are described in the literature, including those reported on by Ingraham and Scott, D'Errico, Shyrock, Moore, Steele, and Walsh [22]; these cases have not otherwise been cited in this paper. In this group of 40 patients there has been a fair degree of regularity in clinical pattern. The more frequently recurring symptoms and signs are listed in Figure 10.

It is worth noting that about one-half of the patients with headache, usually suboccipital, had exacerbation of pain on movement of the head on the neck, usually referred to as "stiff neck." The pain is ordinarily described as radiating in the second cervical root distribution. It is possible that the incidence of sensory abnormality would have been higher had the second cervical region been checked more routinely for isolated sensory loss.

Overt evidence of anomalous development was present in only six of the patients. On the other hand, roentgenologic evidence of associated anomaly of skull or spine was frequent, being mentioned in 23 cases. Platybasia was the most frequent finding, present in 20 cases.

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20. Gardner, W. J., and Goodall, R. J.: The Surgical Treatment of Arnold-Chiari Malformation in Adults, J. Neurosurg. **7**:199-206, 1950.

21. List, C. F.: Neurologic Syndromes Accompanying Developmental Anomalies of Occipital Bone, Atlas and Axis, Arch. Neurol. & Psychiat. **45**:577-616 (April) 1941.

22. Ingraham, F. D., and Scott, H. W., Jr.: Spina Bifida and Cranium Bifidum: V. The Arnold-Chiari Malformation: A Study of 20 Cases, New England J. Med. **229**:108-114, 1943. D'Errico, A.: The Surgical Treatment of Hydrocephalus Associated with Spina Bifida, Yale J. Biol. & Med. **11**:425-430, 1939. Shyrock, E. H.: Complete Obstruction of the Cerebral Aqueduct Associated with Lumbar Meningocele, Bull. Los Angeles Neurol. Soc. **9**:163-166, 1944. Moore, A.: Arnold-Chiari Malformation, Bull. Vancouver Med. A. **21**:108-111, 1945. Steele, G. H.: The Arnold-Chiari Malformation, Brit. J. Surg. **34**:280-282, 1947. Walsh, F. B.: Neuro-Ophthalmology, Baltimore, Williams & Wilkins Company, 1947.

Spinal fluid studies occasionally demonstrated partial or complete block, with protein levels up to 100 mg. per 100 cc. reported.

Ventriculography has not helped appreciably in the specific diagnosis. Pneumoencephalography may demonstrate absence of ventricular filling, but this finding occurs too often in "normal" persons undergoing pneumoencephalography to be of much value.

A definite diagnosis can be made myelographically; with myelography the features of the malformation can be clearly demonstrated and evaluated. Myelographic studies have been reported by List,[21] Epstein,[23] and Lewin, Wycis, and Young.[19] We feel that myelography is the procedure of choice when this condition is suspected.

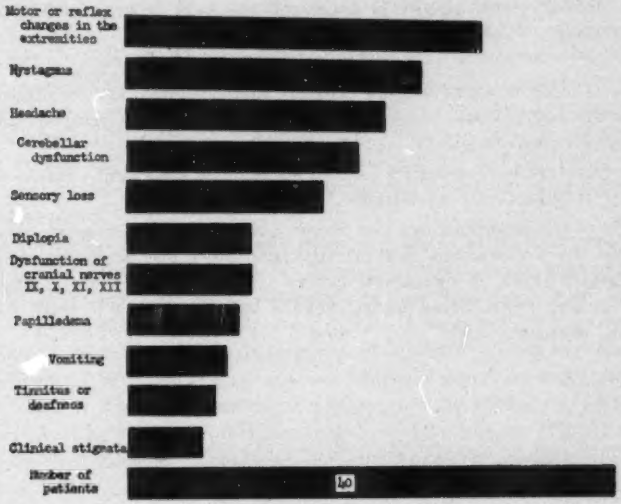

Fig. 10.—Chart showing occurrence of signs and symptoms in 40 cases of Arnold-Chiari malformation.

SURGICAL THERAPY

It now appears that an adult or adolescent patient with the Arnold-Chiari malformation can be offered a relatively good prognosis by proper surgical treatment.

We believe the operative intervention can be done with a vertical midline incision. Overextension of the head for purposes of administration of the anesthetic agent by endotracheal intubation is to be avoided, as is a position of too great flexion during the operation. Moderate suboccipital craniectomy and upper cervical laminectomy should be performed. The lower level of laminectomy can be predetermined by myelography and should be at least one segmental arch below the lower edge of the malformation. The dura should be widely opened and left open; we do not believe that any further intradural procedure is ordinarily needed. Sepa-

23. Epstein, B. S.: Pantopaque Myelography in the Diagnosis of Arnold-Chiari Malformation Without Concomitant Skeletal or Central Nervous System Defects, Am. J. Roentgenol. **59**:359-364, 1948.

ration of adhesions or freeing or resection of the cerebellar tongues is fraught with danger of damage to the underlying medulla or its blood supply.

We believe that relief of obstruction of cerebrospinal fluid pathways, if present, will be accomplished by the decompression. Opening of such channels by cutting adhesions is more likely to result in increased scarring.

We refrain from tapping or incising any cervical or cervicomedullary cysts or nodules. These are most likely to be either the fourth ventricle or a dilated communicating central canal, emptying of which is not indicated; it would appear best to avoid the additional trauma.

Prior to closure, the adequate extent of laminectomy can be noted by extension of the head, as suggested by Hurteau.[15]

The ordinary layer closure is done, and the head is supported by a heavy collar dressing.

SUMMARY

Reports of three adults with the Arnold-Chiari malformation are presented. In all three the diagnosis was suggested clinically, substantiated myelographically, and successfully treated surgically.

The literature is reviewed; a total of 40 adult or adolescent patients is noted, and their syndromes are summarized.

Study of the reported cases and of our own material led to expression of our belief that the malformation is a primary anomaly of the hindbrain, rather than the secondary result of mechanical factors. An attempt is made to review the clinical features which should aid in diagnosis and to suggest a logically restrained operative treatment.

ANATOMIC STUDIES ON THE SYMPATHETIC NERVOUS SYSTEM

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LAWRENCE, KAN.

RECENT advances in surgery make approaches to the sympathetic nervous system more feasible than ever before. Indications for sympathetic nerve surgery and the results of operations depend on fundamental knowledge of the anatomy and physiology of the sympathetic nerves. This morphologic study of the thoracolumbar sympathetic chains and rami was carried out to compare the findings with descriptions in standard anatomy textbooks and to contribute knowledge leading toward effective sympathetic denervation and prevention of nerve regeneration. The thoracic and lumbar sympathetic chains were carefully dissected and drawn in detail in adult human cadavers, 41 of the best bilateral dissections being used as the basis for this paper.

The embryology of the sympathetic chain is reflected in adult anatomy. The solid mass of neural crest cells does not consistently differentiate into a ganglion for each body segment, and sympathetic ganglions sometimes supply more than one segmental nerve in the thoracic and lumbar regions (always in the cervical region). In the upper four and lower two thoracic segments communicating rami from one ganglion frequently were found supplying more than one intercostal nerve; however, there were almost always the same number of ganglions as nerves, the dual supply being due to arching of rami in two directions from the ganglions (Figs. 1 and 2). At times the chain assumed a broad form, the ganglions being difficult to distinguish as separate bodies. In such cases the adult arrangement resembled that found in dissections of small fetuses which were carried out parallel with the present study on adults. The fetal chain was found to be almost ribbon-like and the ganglions almost touching one another, growth and differentiation normally producing elongation with separation of the ganglionated masses of cells and relative decrease in size of the chain between ganglions. Failure of definite ganglion formation was not unusual and was commonly found in the region between the eleventh thoracic and first lumbar ganglions where the chain was frequently broadened in lieu of a twelfth ganglion (Fig. 2).

It has been shown that early in the embryo, sympathetic ganglions differentiate in close association with segmental arteries, some of which disappear later.[1] In this study, the close association of sympathetic nerve tissue with blood vessels in the adult was impressive. Rather sizable rami from the thoracic chain accompanied intercostal arteries to the aorta, and large rami converged to run on the azygous,

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1. Morin, P. F.: Recherches sur la morphologie et la morphogènèse du sympathique cervical, Acta anat. **2**:351, 1947.

accessory hemiazygous and hemiazygous veins in some specimens (Fig. 1). An anomaly was noted in which the right second intercostal vein was lateral to the chain three times, the right third intercostal ten times, and the right fifth intercostal one time. On the left the variation was found only once, with the third intercostal vein.

The thoracic ganglions were found beneath the pleura on the heads of the ribs or between the ribs, with the ganglion lying on the head of the rib below the intercostal nerve to which it corresponded, or in the same interspace with it. No significant differences in male and female chains were noted except that often the female chain and ganglions were extremely small. At the level of the eleventh interspace or the head of the twelfth rib the eleventh ganglion was the last truly thoracic part of the chain. It was often closely associated with the pleural reflection or the

Fig. 1.—*SG* indicates stellate ganglion; *NI*, first thoracic nerve; *C*, communication between first and second thoracic nerves; *IA*, intercostal artery; *CR*, communicating ramus from sympathetic ganglion to intercostal nerve; *Az*, azygous vein; *SR*, sympathetic ramus following azygous vein; *IR*, sympathetic ramus following aortic intercostal artery, and *SC*, sympathetic chain. Note the position of the third intercostal vein lateral to the sympathetic chain.

Fig. 2.—Right lower thoracic and upper lumbar sympathetic chain showing widening of chain between the eleventh thoracic and the first lumbar segment in lieu of a twelfth ganglion. Note that the tenth and eleventh thoracic segments are connected with two segmental nerves by communicating rami.

origin of the crus of the diaphragm. From the eleventh ganglion caudad, the sympathetic chain turned rather abruptly forward on the bodies of the vertebrae. In 22% of dissections on the right and 24% on the left, the chain became flat and ribbon-like at the eleventh ganglion. In such cases the twelfth ganglion was usually indistinguishable per se (Fig. 2). In other specimens the chain narrowed after the eleventh thoracic segment and a definite twelfth ganglion was present (42% on the right and 54% on the left). In such cases the twelfth ganglion was usually not half the size of the eleventh (Fig. 3). It was buried within the origin of the diaphragmatic crus. In 24% of dissections on the right and 12% on the left the twelfth ganglion and first lumbar ganglion were combined, in which case the communicating rami to the twelfth nerve came off either the narrow chain or the combined ganglion (Fig. 4).

Several other variations occurred in the remaining 12% on the right and 10% on the left, including fusion of the eleventh and twelfth ganglions, the occurrence of two ganglions or a double ganglion supplying the eleventh and/or twelfth nerves, and absence of the tenth or eleventh ganglion.

The chain could easily be lost between the eleventh and twelfth ganglions in those cases in which it became narrow at that point and between the twelfth and first lumbar ganglions, where 27% of the right and 24% of the left chains were very narrow (Fig. 3). Incorporation of the chain in the crus of the diaphragm and in tendinous origins of the psoas muscles, which sometimes overlapped the chain, interfered with rapid identification of continuity in these dissections. This promotes the ease with which the lesser splanchnic nerve may be mistaken for the sympathetic chain at this point during a surgical procedure.

Fig. 3.—Right lower thoracic and upper lumbar sympathetic chain showing the presence of a twelfth sympathetic ganglion.

Fig. 4.—Right lower thoracic and upper lumbar sympathetic chain showing fusion of the twelfth and first ganglions.

In the lumbar region, variation in number, size and form of ganglions was found, as reported previously by others.[2] In one dissection on the right and two on the left the lumbar chain was broad and flat. A few lumbar veins were demonstrated lying lateral to the chain in a manner similar to that found in the upper thoracic region.

Usual textbook descriptions of the splanchnic nerves state that the greater splanchnic nerve arises from the fifth to the tenth thoracic ganglion,[3] sends branches

2. (*a*) Kuntz, A.: The Neuroanatomic Basis of Surgery of the Autonomic Nervous System, Springfield, Charles C Thomas, Publisher, 1949. (*b*) Morris, H.: Human Anatomy, ed. 10, Philadelphia, The Blakiston Company, 1942.

3. (*a*) Gray, H.: Anatomy of the Human Body, ed. 25, Philadelphia, Lea & Febiger, 1948. (*b*) Kuntz.[2a] (*c*) Morris.[2b]

to the aorta, esophagus and thoracic duct,[2b] and terminates in the celiac ganglion [2]; that the lesser splanchnic nerve arises from the ninth or tenth ganglion [2] and sometimes the eleventh [3a] and terminates in the aorticorenal ganglion,[4] celiac ganglion and renal plexus [2b] and that the lowest splanchnic nerve arises from the last thoracic ganglion [3a] or lesser splanchnic nerve [2] and terminates in the renal plexus.[5]

This study demonstrated variations from the above descriptions and additional pathways, showing that the anatomy of the splanchnic nerves is atypical of any one description. A classification consisting of three types was formulated, into which 88% of splanchnic nerves on the right and 90% on the left could be placed in this series of dissections. The most frequent type to occur, Type I (Fig. 5), showed a structure usually considered to be the greater splanchnic nerve arising as high as the third thoracic ganglion and as low as the tenth and sometimes the eleventh thoracic ganglion, actually representing a combination of the greater and lesser splanchnic nerves. It is believed that the roots from the tenth and eleventh ganglions in this type represent the lesser splanchnic nerve. The combined structure, after sending rami to the aortic plexus, terminated in the lateral part of the celiac ganglion, usually sending some fibers directly through the ganglion to the renal and aortic

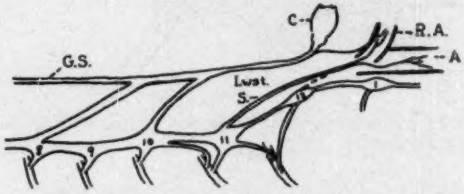

Fig. 5.—Type I splanchnic nerve arrangement showing fusion of the greater and lesser splanchnic nerves, occurring in 39% of 41 dissections on the right and in 41% on the left. *G.S.* indicates greater splanchnic nerve; *C*, celiac ganglion; *R.A.*, renal artery; *A*, aorta, and *Lwst. S.*, lowest splanchnic nerve. The broken line represents alternate origin of lowest splanchnic nerve.

plexuses. Here again, the continuing fibers probably represented the lesser splanchnic nerve component. In two dissections on the right and five on the left, the tenth or eleventh ganglion supplied rami to both a combined greater and lesser splanchnic nerve and a combined lesser and lowest splanchnic structure. These specimens are represented by adding the broken line to Figure 7.

Almost as frequent in occurrence, Type II (Fig. 6) showed the greater, lesser and lowest splanchnic nerves as separate structures but still having communications with one another. When occurring alone, the greater splanchnic nerve arose as high as the third and as low as the ninth thoracic ganglion, terminating in the lateral portion of the celiac ganglion after sending rami to the aortic plexus. The lesser splanchnic nerve arose from the tenth or eleventh thoracic ganglion, rarely the ninth, and terminated in the renal and aortic plexuses. The lowest splanchnic nerve arose from the eleventh and/or twelfth ganglion and terminated chiefly in the aortic plexuses and associated ganglions, supplying a few fibers to the renal plexus. In four dissections the lowest splanchnic nerve terminated directly in the superior mesenteric plexus.

4. Kuntz.[2a] Gray.[3a]
5. Kuntz.[2a] Morris.[2b] Gray.[3a]

The least common splanchnic nerve arrangement, Type III (Fig. 7), showed the greater splanchnic origin and termination similar to that in Type II, with fusion of the lesser and lowest splanchnic nerves into one structure which terminated in the renal and aortic plexuses. It was mentioned above that fusion of the lowest and a portion of the lesser splanchnic nerves was seen also in some of the dissections grouped under Type I.

The specimens not falling into the three general types included two right and two left dissections in which the greater, lesser and lowest splanchnic nerves were combined into one structure terminating in the lateral portion of the celiac ganglion and sending secondary rami to the renal and aortic regions. One on the right and two on the left were a combination of Types I and II. Only two other dissections, both on the right, were not classified.

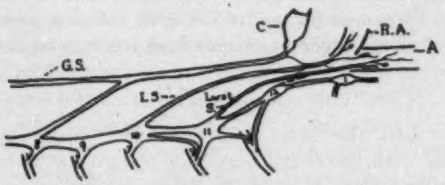

Fig. 6.—Type II splanchnic nerve arrangement showing separate greater, lesser and lowest splanchnic nerves, occurring in 22% of 41 dissections on the right and in 39% on the left. Note the communcations between the splanchnic nerves. *G.S.*, indicates greater splanchnic nerve; *L.S.*, lesser splanchnic nerve; *Lwst.S.*, lowest splanchnic nerve; *C*, celiac ganglion; *R.A.*, renal artery, and *A*, aorta. The broken line represents alternate origin of lowest splanchnic nerve.

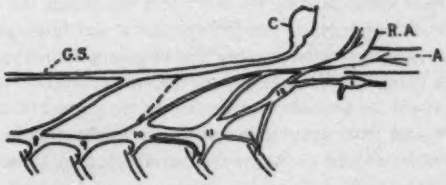

Fig. 7.—Type III splanchnic nerve arrangement showing fusion of the lesser and lowest splanchnic nerves occurring in 27% of 41 dissections on the right and in 10% on the left. *G.S.* indicates greater splanchnic nerve; *C*, celiac ganglion; *R.A.*, renal artery, and *A*, aorta.

The term "renal plexus" used here includes small ganglions in apposition to the renal artery but separate from other ganglions. Small ganglions, in which the lesser and lowest splanchnic nerves often terminated, occurred in a scattered manner down the dorsal, ventral and lateral aortic regions. The term "aorticorenal ganglion" is not used in this paper since the existence of such a structure was found to be so inconstant and variable. No such termination was found to be typical of the lesser splanchnic nerve, which usually leads directly into small, irregular, independent ganglions about the renal artery or into the celiac ganglion in conjunction with the greater splanchnic nerve. If one were obliged to use the term "aorticorenal" in classifying this material, it would be necessary to state that the greater splanchnic nerve often terminated in such a structure. It is probable that fusion of the greater and lesser splanchic nerves influences the termination of the greater splanchnic

nerve. Statements that the greater splanchnic nerve arises as low as the tenth ganglion are probably based on instances in which the greater and lesser nerves are fused (Fig. 5). In only 2% of dissections on the right and 7% on the left in this study did the lesser splanchnic nerve arise from the ninth ganglion in whole or in part. In addition to splanchnic roots, independent rami from the tenth and eleventh ganglions were found going directly to the aortic plexus.

The manner in which the splanchnic nerves and sympathetic chain pierce the diaphragm has been reported to vary. It has been stated that the greater splanchnic nerve passes through the aortic hiatus on the left in 6 to 20% of dissections.[6] In no case in this series did a greater splanchnic nerve fail to pierce the crus of the diaphragm. The greater splanchnic was lateral to the lesser and lowest splanchnic nerves and the sympathetic chain, which were closely applied to the vertebral bodies, but pierced the crus in individual places. Sometimes the different structures were separated by only a few muscle fibers and at other times by sizable portions of the crus; but they were always found in separate compartments formed by some portion of the diaphragm.

COMMENT

It can be postulated that fibers from the upper thoracic segments, following intercostal arteries, with downward angulation toward the aorta, may form conduction pathways with fibers at lower levels and that the aortic plexus in general may take part in substitution or regeneration of sympathetic function in regions where the chain has been resected. It has been stated that there is sometimes a para-aortic nerve and that resection as high as the fourth ganglion would render this structure nonfunctional.[7] The present study has demonstrated large fibers from the sympathetic chain accompanying the third and sometimes the second intercostal artery (highest aortic intercostal) toward the aorta and large rami from as high as the first thoracic ganglion accompanying the accessory hemiazygous, hemiazygous and azygous veins. This would suggest that removal of the third or occasionally the second ganglion would be necessary to render aortic pathways devoid of thoracic sympathetic fibers and that, even then, pathways might still be functional along veins. Microdissection should show even more fibers than those demonstrated in this study.[8]

Attention has been called here to the high origin of the greater splanchnic nerve in a few cases. This has been reported by others.[9] Long communicating rami between ganglions and segmental nerves in both the upper and the lower thoracic regions offer pathways which may be missed during concentration on removing only the chain and ganglions (Figs. 1 and 2). Broad ribbon-like chains may easily be split, a few fibers being left behind. Frequently there is loop formation at natural

6. Näätänen, E. K.: (*a*) Über die Anatomie des Truncus sympathicus thoracicus bei Neugeborenen und Feten, Acta Soc. med. fenn. duodecim (Ser. A, fasc. 3) **23**:15, 1947; (*b*) Beiträge zur Kenntnis der Anatomie der Nervi splanchnici, Acta Soc. med. fenn. duodecim (Ser. A, fasc. 3) **23**:1, 1947.

7. Mitchell, G. A. G.: An Anatomical Evaluation of Operations for Hypertension, Edinburgh M. J. **44**:545, 1947.

8. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System, ed. 2, New York, The Macmillan Company, 1941.

9. Näätänen.[6a] Mitchell.[7]

splitting of the chain for one or more segments. Such loops might be overlooked during operations. Possible sympathetic pathways via the phrenic and vagus nerves to the adrenal glands, celiac plexus and thence other abdominal regions have been demonstrated.[7] Aberrant small ganglions of sympathetic nerve tissue have been described, most commonly occurring in the cervical region and on the roots of the first and second intercostal nerves and the first and second lumbar nerves.[10] Removal of the sympathetic chain and splanchic nerves would not eliminate these structures.

The relative size of the sympathetic chain in different regions should be a gross measure of concentration of preganglionic and postganglionic fibers. Since one preganglionic neuron apparently activates many cell bodies of postganglionic neurons,[11] the chain is of relatively greater size in the upper and lower thoracic regions. In some dissections the chain is wide in only the upper three or four thoracic segments. In others it may be relatively wide as low as the sixth or seventh segments. It is postulated that since afferent and efferent systems arise segmentally in conjunction with one another in the embryo, ganglionectomy for relief of angina pectoris might be required at a lower level in patients showing a broad chain with large ganglions below the fourth or fifth thoracic level than the usual patient with concentration of nerve tissue at a higher level. The small size of the cervical and lumbar chains, except for their ganglions, also conforms with the principle of many postganglionic nerves from few preganglionic fibers.

The termination of part of the lesser and the lowest splanchnic nerves in the aortic plexus, as pointed out in this study, may have considerable significance. Some may be primarily involved in lymphatic physiology since many nerve fibers commonly terminate in the region of the cisterna chyli. Their function remains to be demonstrated.

SUMMARY

Forty-one bilateral dissections of the thoracic and lumbar sympathetic chains and some of their rami are reported and classified by division into three principal groups.

The greater splanchnic nerve was found to arise from as high as the third and as low as the ninth thoracic sympathetic ganglion and, after sending rami to the aortic plexus, to terminate in the lateral part of the celiac ganglion.

The lesser splanchnic nerve was found to arise usually from the tenth, but sometimes the eleventh, and seldom the ninth thoracic sympathetic ganglion and to terminate in the renal and aortic plexuses.

The lowest splanchnic nerve was found to originate in the eleventh or twelfth ganglion and to terminate mainly in the aortic plexus and small associated ganglions, few fibers reaching the renal plexus.

Fusion of the greater and lesser splanchnic nerves into one structure, with termination in the lateral part of the celiac ganglion, was found more frequently than the occurrence of these nerves alone (39% on the right and 41% on the left);

10. Skoog, T.: Ganglia in the Communicating Rami of the Cervical Sympathetic Trunk, Lancet **2**:457, 1947. Alexander, W. F.; Kuntz, A.; Henderson, W. P., and Ehrlich, E.: Sympathetic Ganglion Cells in Ventral Nerve Roots: Their Relation to Sympathectomy, Science **109**:484, 1949.

11. Wolf, G. A., Jr.: The Ratio of Preganglionic Neurons to Postganglionic Neurons in the Visceral Nervous System, J. Comp. Neurol. **75**:235, 1941.

fusion of the lesser and lowest splanchnic nerves was found in 27% on the right and 10% on the left, and fusion of the greater, lesser and lowest splanchnic nerves was found in 5% bilaterally. Where fusion was found, structures ordinarily supplied directly by the components of the fused nerve were usually supplied secondarily by direct passage of fibers through the terminal ganglion.

The splanchic nerves and sympathetic chain pierced the crus of the diaphragm in separate irregular compartments in every dissection, none traversing the aortic hiatus.

Possible pathways of nerve function and regeneration following some thoracic and lumbar sympathetic denervation procedures are postulated and reviewed briefly.

Branches of the splanchnic nerves to the aortic plexus are emphasized.

The ease with which the lesser splanchnic nerve may be mistaken for the sympathetic chain during splanchnicectomy is pointed out.

PRODUCTION OF EXPERIMENTAL CRETINISM IN DOGS BY THE ADMINISTRATION OF RADIOACTIVE IODINE

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CRETINISM has been produced experimentally in rabbits,[1] sheep and goats,[2] and swine[3] by surgical removal of the thyroid glands. The feeding of thiouracil to pregnant rats was found to cause retardation of growth and in the development of the bones, mild anemia, and thyroid hyperplasia in the young.[4] Attempts to produce cretinism in dogs by surgical removal of the thyroid glands have usually failed because of injury or removal of the closely associated parathyroid glands.

It is the purpose of the present report to record the complete destruction of the thyroid gland in new-born puppies by the administration of radioactive iodine (I^{131}), with subsequent development of cretinism. Radioactive iodine was given to pregnant bitches near term or to pups at varying intervals after delivery. The mother was permitted to nurse and care for the young, and an attempt was made to preserve 50% of the litter as a control. There were, of course, no controls for the pups that received I^{131} in utero as a result of injection of the mother. From time to time estimations were made of the total serum lipids, proteins, glucose, and calcium. Thyroid function was estimated by determination of the conversion ratio of free to protein-bound iodine after the method of Clark.[5] Clark found that when radioactive iodine is administered orally in man and the blood examined after 24 hours, from 13 to 42% of the total blood iodine is in the protein-bound fraction and the remainder in the filtrate. When more than 50% of the radioactive iodine of the blood appeared in the protein-bound fraction, a diagnosis of hyper-

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1. Basinger, H. R.: The Control of Experimental Cretinism, Arch. Int. Med. **17**:260 (Feb.) 1916.

2. Liddell, H. S., and Simpson, E. D.: The Onset of the Pot-Belly in Thyroidectomized Sheep and Goats, Am. J. Physiol. **76**:195, 1926.

3. Caylor, H. D., and Schlotthauer, C. F.: Cretinism and Myxedema Produced Experimentally in Swine, Am. J. Physiol. **79**:141, 1926.

4. Hughes, A. M.: Cretinism in Rats Produced by Thiouracil, Endocrinology **34**:69, 1944.

5. Clark, D. E.; Moe, R. H., and Adams, E. E.: Rate of Conversion of Administered Inorganic Radioactive Iodine into Protein-Bound Iodine of Plasma as an Aid in the Evaluation of Thyroid Function, Surgery **26**:331, 1949.

thyroidism was made, whereas when less than 10% of the blood iodine appeared in the protein-bound fraction the patient was considered to have hypothyroidism. The latter figure was obtained for patients with myxedema following thyroidectomy for carcinoma or from destruction of the thyroid gland by carcinoma.

PROTOCOLS

Dog 85, a brown male, was whelped on Aug. 26, 1948, by a brown and white short-haired hound bitch, paternity unknown. On the second day of life he was given 0.5 mc. (Oak Ridge standard) of radioactive iodine (I^{131}) subcutaneously. At the age of 4 months the conversion

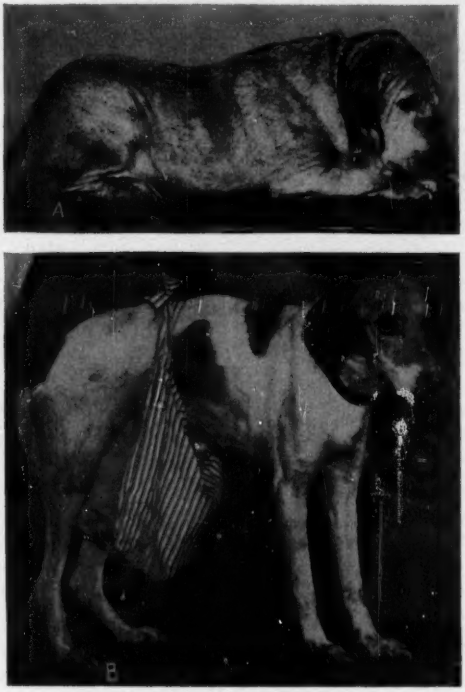

Fig. 1.—*A*, Dog 85, one-year-old cretin dog, treated with 1½ mc. I^{131} shortly after birth, in his characteristic pose. Note the redundant skin, broad body, and short extremities. *B*, Dog 52, normal dog, mother of Dog 85, with a gastric fistula.

ratio of free to protein-bound iodine of the plasma was 40%, indicating normal thyroid function. A second version ratio at 7 months of age was 6%, or within the hypothyroid range from clinical experience. An additional dose of 1.0 mc. of radioactive iodine was given on April 21, 1949, when the dog was 8 months of age, so that the total dose of radioactive iodine administered to this animal was 1.5 mc.

Although as a young puppy Dog 85 was normally active, at the age of 2 months distemper developed, and his behavior could not be accurately gauged. Immediately after his recovery he was again active; however, he became progressively more lethargic and at the end of 4 months appeared definitely abnormal. He had short, bowed legs. His skin was thickened, tough, and

dry, and his hair was coarse. After a second dose of I^{131} at 8 months of age, these findings became gradually more marked. His abdomen was broad and protuberant. He never barked, and he remained in one position for many hours. When placed in awkward positions, such as on his back, he made no effort to right himself. His skin was redundant, especially about his face, and he was expressionless. For a comparison of this dog and his mother, see Figure 1.

Chemical examination of the blood was made at regular intervals. The serum cholesterol was normal at 2 months, but from the age of 4 months it was persistently elevated, reaching a maximum of 565 mg. per 100 cc. on May 11, 1949. Likewise, the total serum lipid values were high, ranging from 1,035 to 2,590 mg. per 100 cc. (600 to 900 mg. is normal by our methods). The alkaline phosphatase was increased to 19 mg. per 100 cc. at the age of 6 months but thereafter was within the normal range. Serum protein, glucose, and calcium levels were always normal (Table).

Blood Chemical Data on Cretin Dog 85

Date	Serum Lipids, Mg./100 Cc.	Alkaline Phosphatase, Units/Cc. of Serum	Cholesterol, Mg./100 Cc.	
			Free	Total
10/31/48	.....	....	85	100
2/ 1/49	1,035	....	137	362
2/17/49	1,081	10.6	195	443
3/ 2/49	1,320	7.9	...	...
3/16/49	1,690	18.9	137	394
3/30/49	1,765	10.8	...	...
4/13/49	2,150	8.7	180	486
4/27/49	2,015	11.1	...	...
5/11/49	2,290	8.5	116.5	565
5/25/49	2,050	10.2	...	...
6/ 8/49	2,410	8.9	205	357
6/22/49	2,120	7.6	...	...
7/ 7/49	2,215	8.3	102	374
7/20/49	1,660	4.7	...	...
8/ 3/49	1,560	4.0	145	550
8/17/49	1,700	5.2	...	...
8/31/49	1,925	2.5	150	581
9/13/49	1,922	4.3	...	...
10/ 5/49	1,635	3.1	...	...
10/18/49	1,810	4.1	137.5	480
11/ 1/49	1,987	4.3	...	...
11/16/49	2,590	3.5	...	...
11/23/49	liver 26% fat by weight	....	...	...

This dog died on Nov. 17, 1949, the second day after pancreatectomy, from pneumonia. In the neck no thyroid tissue was found on gross or microscopic examination. The parathyroids were not identified.

The subcutaneous fat was plentiful over the entire body and was 8 mm. thick over the abdomen. The omentum and the retroperitoneal tissues contained large fat deposits. The testes were small, and no spermatogenesis was present. No abnormalities were noted in the pancreas or the adrenal glands. The pituitary appeared slightly enlarged. The liver showed focal fatty changes and contained 26% fat by weight.

Dog 145, a light brown male, and Dog 146, a light brown female, were whelped on May 27, 1949, by a part-collie mongrel bitch, paternity unknown. The male was given 0.6 mc. of I^{131} on June 17, 0.5 mc. on July 19, and 1.0 mc. on August 29, making a total of 2.1 mc. At 10 weeks it was noted that the control female was definitely larger and more active (Fig. 2) and this became progressively more marked until their death on November 25. Dog 145 resembled Dog 85 in appearance, having very coarse, dry hair, and a wrinkled dry skin. His legs were short and bowed, and his forelegs were puffy. The abdomen was broad and protuberant. He also did not bark and lay for hours with his head between his forepaws. A conversion ratio of free to protein-bound iodine on November 17 was 5.5%.

Serum chemistry determinations were made at regular intervals in each dog. Although the serum lipids were normal in each, they were definitely higher in Dog 145. The alkaline phosphatase was also higher in this animal. The serum cholesterol was not significantly different.

Roentgenograms were taken of the right foreleg at the age of 4½ months. In each six centers of ossification were present in the carpal bones. However, in the iodine-treated dog the centers of ossification were much smaller than in the control, and the wrist joint was almost entirely cartilage. In the long bones (radius, ulna, humerus, and metacarpals) the length was about one and a half times as great in the normal as in the treated dog. The shafts were the same width in each. The secondary centers of ossification were much farther advanced in development in Dog 146, the control. The secondary center of ossification for the olecranon was well developed in Dog 146 and not yet present in Dog 145.

Dog 145 died on Nov. 25, 1949, and Dog 146 was killed for control studies. The cause of death in the cretin was a perforated duodenal ulcer with generalized peritonitis. Dog 145 weighed 7.4 kg., had a length of 57 cm., and a shoulder height of 36 cm. Comparative measurements for the normal control were 16.7 kg., 76 cm., and 50 cm. On examination of the neck of the cretin

Fig. 2.—Dog 146, control female, and, on the right, Dog 145, a male, treated with I^{131} one day after birth. Pictures taken when these dogs were 10 weeks old show disparity in size.

for thyroid tissue, none was found. Two of the parathyroid glands were identified as yellow bodies 1 to 2 mm. in diameter. On microscopic examination the only abnormality was a slight increase in fibrous tissue. No abnormalities were found in the heart, lungs, great vessels, liver, adrenals, and skin. The testes showed no spermatogenesis. The hypophysis in Dog 145 was enlarged.

Detailed bone studies were made on these two animals. In the iodine-treated dog the patella was entirely cartilage, while in the control it was well ossified. The epiphysis for the greater trochanter was not present in the treated dog, and the capital femoral epiphysis was poorly developed (osteoid well formed only in focal areas). In the normal animal the capital epiphysis showed much greater development, and the epiphysis for the greater trochanter was present. There was rapid growth and deposition of osteoid at the epiphyseal line. (See Figs. 3, 4, 5, and 6 for photomicrographs of the bones.) Similar findings were also present in the humeri and tibiae. In summary, the diaphyses were approximately the same in the iodine-treated animals as in the control, but the epiphyses appeared later and developed slower. In addition, there was not the orderly laying down of osteoid at the epiphyseal lines in the iodine-treated animals.

Stock Dog 210 whelped six pups on Nov. 16, 1949. Two were taken as controls, and four were given a total of 3.0 mc. of radioactive iodine each in divided doses on November 17,

Fig. 3.—Photomicrograph of proximal end of femur in Dog 146, showing well developed capital femoral epiphysis and epiphysis for greater trochanter.

Fig. 4.—Proximal femur in cretin Dog 145, showing poorly developed capital femoral epiphysis and absent epiphysis for greater trochanter.

December 8, January 19, and February 16. One of the controls died of a large pericardial cyst on Feb. 20, 1950. The other was noted to be larger and more active than the radioactive iodine-treated litter mates as early as six weeks after birth, and this difference became progressively

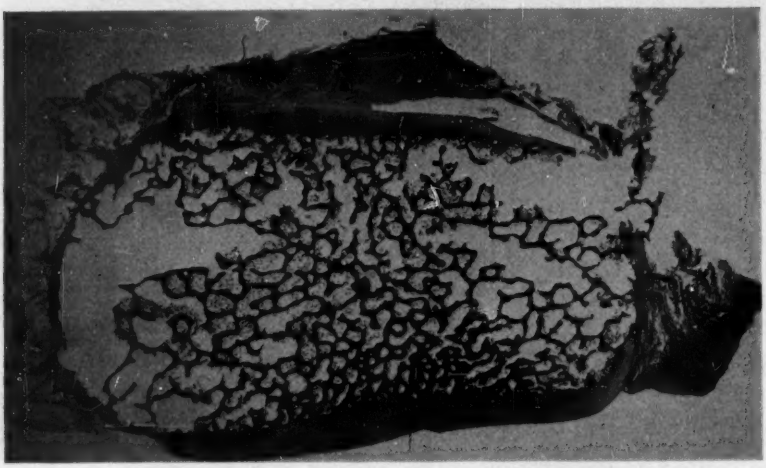

Fig. 5.—Patella of Dog 146, normal control, showing advanced stage of ossification.

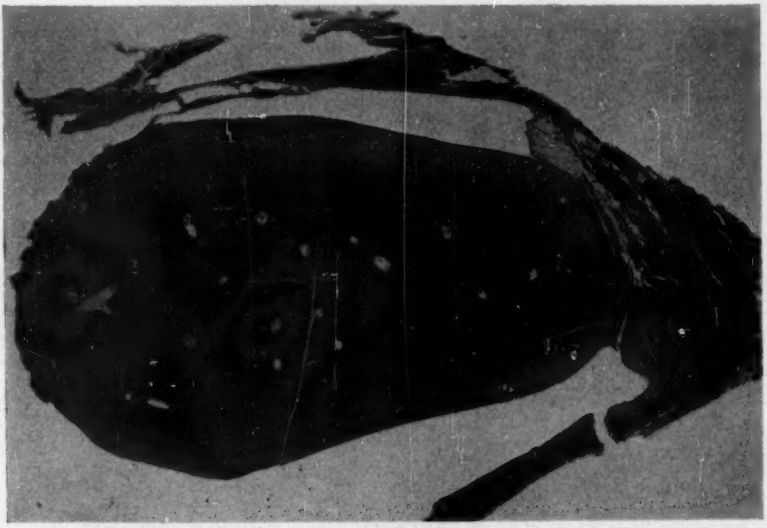

Fig. 6.—Patella of cretin Dog 145, showing very early ossification, with the majority of the bone still cartilage.

more marked. Two of the radioactive iodine-treated animals died at 4 months of age from pneumonia. Three parathyroid glands were identified in each at autopsy, but no thyroid remnant was found in either. The other endocrine glands appeared normal.

Conversion ratios done on the surviving radioactive iodine-treated dogs were between 4.1 and 6.6 for one and 9.5 and 3.2 for the other. A conversion ratio done on the normal litter mate was 27.8, a euthyroid level. Serum cholesterol determinations, done at monthly intervals beginning Jan. 10, 1950, in the normal, have varied between 121 and 277 mg. per 100 cc. The level in the iodine-treated litter mates has always been higher, the maximum being 475 mg. in one and 575 mg. in the other. The total serum lipids have likewise been increased in these dogs, varying between 1,120 and 1,675 mg. per 100 cc. in one and between 1,263 and 1,800 mg. in the other. The level in the control has been normal (Fig. 7*A*).

There have also been marked differences in the skeletal development. Roentgenograms of the forelegs taken when this litter was 4 months of age revealed the secondary centers of ossification to be much better developed in the normal than in the radioactive iodine-treated litter mates. The epiphysis for the olecranon was well developed in the normal and had not appeared in the

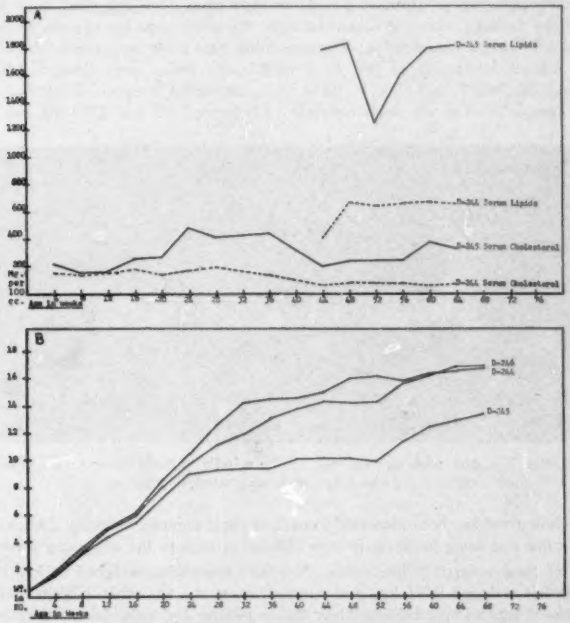

Fig. 7.—*A*, curves showing elevated serum lipids and cholesterol in cretin Dog 245 as compared with normal litter mate Dog 244. *B*, growth curve litter No. 210. Dog 246 and Dog 245 received 3.0 mc. of radioactive iodine in divided doses. Their rate of growth lagged behind untreated litter mate Dog 244 despite heavy fat deposits.

treated dog. Six carpal bones were present in each but were much better developed in the normal animal. The length of the radius and ulna and of the metacarpal bones in the normal was about one and a half times the length of that in the radioactive iodine-treated dog, although the width was the same in each. Repeat roentgenograms taken at the age of 15 months revealed that in the normal dog the distal radial and ulnar epiphyseal lines were almost closed. The metacarpal bones in the normal dog were one and a half times the size of the corresponding carpal bones in the treated dogs. In the latter the distal radial and ulnar epiphyses were open at 15 months.

These dogs, now 16 months of age, vary greatly in their appearance (Fig. 8). The control is rangy and lean, with long, slender extremities. He is alert and active. The radioactive iodine-

treated animals are approximately two-thirds as tall as he at the shoulder but are much broader through the chest and abdomen. They have heavy subcutaneous fat deposits and a dry, tough, loose skin. Their hair is coarse and dry. Their legs are short, stubby, and bowed. Their lower jaws are prominent, and the lower teeth protrude even with the mouth closed. The tongue is large and is protuberant in each. The animals are lethargic, do not bark, and lie for hours in the same position. (See Fig. 7*B* for rate of growth.)

These findings led us to believe that it might be possible to produce cretinism in utero, since it is known that iodine crosses the placental barrier. Dog 267, a large, white mongrel weighing 20 kg., was given 15.4 mc. of radioactive iodine on Nov. 29, 1949, and on December 2 delivered nine viable puppies. These appeared less active than normal from the time of birth and nursed poorly. Nevertheless, six survived the neonatal period; three dying at the ages of 3, 5, and 3 weeks revealed complete replacement of the thyroid tissue by areolar tissue, with the preservation of normal-appearing parathyroid glands in each case. One dog died of pneumonia at 7 months, and the findings were the same. In each the other endocrine glands appeared normal on gross and microscopic examination. The remaining pups grew very slowly and were lethargic (Fig. 9*A*). Conversion ratios of free to protein-bound iodine were done on these dogs on Jan. 31, March 24, June 7, and Nov. 11, 1950, and have varied between 2.6 and 9.2, all definitely hypothyroid levels. Total serum lipids have varied between 1,025 and 2,513 mg. per 100 cc., and

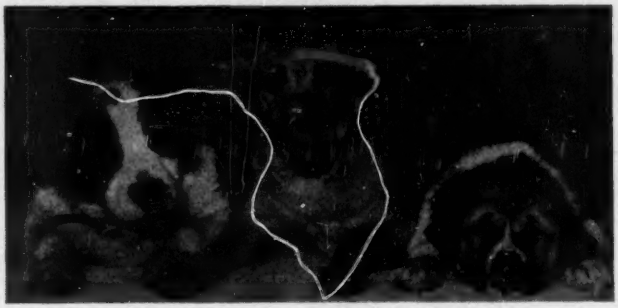

Fig. 8.—Litter No. 210, with normal dog in the middle. Cretin litter mates receiving a total of 3 mc. of I^{131} show coarse hair, short forelegs, and marked prognathia.

total serum cholesterol has been increased in each of these animals, reaching the level of 850 mg. per 100 cc. in one and being persistently over 350 mg. in each of the remaining litter mates.

The size of these animals is interesting. Whereas the mother weighed 20 kg., the most any of these dogs has weighed is 11 kg., and one weighs, at the age of 16 months, only 6 kg. All have short bowed legs and pot bellies. Their skin is coarse, dry, redundant, and extremely tough. They do not play together and are not active, almost never barking. Roentgenograms of these dogs taken at the same age as those in the previous litter reveal the same findings as we have noted in the radioactive iodine-treated dogs; that is, they have a delayed appearance of the olecranon epiphysis and a largely cartilaginous wrist joint at the age of 4 months. At 15 months the epiphyses for the distal radius and ulna are open.

Stock Dog 594 was given 15 mc. of I^{131} on Jan. 9, 1950, and delivered nine feeble puppies on January 19. Four died in the first week, and four more died at 4 to 5 weeks. These pups failed to gain weight, largely because they did not learn how to nurse. Postmortem examination of the pups dying at less than one week revealed almost complete replacement of the thyroid by areolar tissue, small islands of fetal thyroid persisting. In those dying at 4 weeks the thyroid was completely replaced by fat. In each, two to four normal parathyroids were identified. The remaining endocrine organs appeared normal grossly and microscopically.

The one surviving animal gained weight very slowly, reaching a weight of 7.5 kg. on Sept. 11, 1950. From the beginning he was incredibly stupid and had to be fed by hand. He would remain in one place for hours at a time. He never learned to bark. His tongue was protuberant

from the age of 4 weeks; his hair was coarse and dry. His subcutaneous fat was heavy, and he had a pot belly. Conversion ratios were 7.4 on March 24, 1950, and 5.4 on June 7. The total lipid value was 1,207 mg. on September 11, and 1,910 mg. on October 9. Total cholesterol was 295 and 276 mg. on two occasions. On October 11 the dog died from complete intestinal obtsruction, caused by ingestion of wood shavings. Autopsy revealed that the thyroid was absent. Four parathyroids were identified and were normal. The testes showed no evidence of spermatogenesis. Other endocrine glands appeared normal, as did the liver.

Stock Dog 506, a long-haired, white mongrel, was given 15 mc. of I^{131} on Jan. 20, 1950, and on January 29 whelped seven feeble puppies. Two died at one week, and two more at 2 weeks of age. In each there was almost complete replacement of the thyroid gland by areolar tissue, with small islands of surviving fetal thyroid tissue. The parathyroids were identified in each and appeared normal. The other endocrine glands also appeared normal. Another,

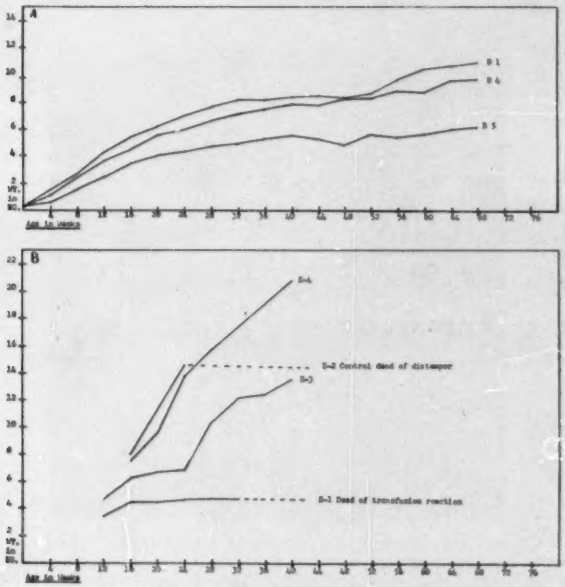

Fig. 9.—*A*, litter No. 267, treated with 15 mc. of radioactive iodine three days prior to whelping. *B*, American bull terrier litter growth curve. E-1 received 1 mc. of radioactive iodine at birth and 1 mc. at 4 weeks. E-3 had 5 mc. of radioactive iodine at 8 weeks and 10 mc. at 6 months. E-2 and E-4 are controls.

a female, died at the age of 11 months from injuries from a fight. No thyroid remnant was found. Four parathyroids were present. The ovaries were immature. The other endocrine organs appeared normal.

The remaining two dogs are now one year old, and weigh 4.9 and 7.6 kg., respectively. In the last four months they have gained 1 kg. apiece only. They have coarse, dry hair, and tough skin with a heavy layer of subcutaneous fat. Each has bowed legs and a pot belly. They do not bark or play together and move about very little.

The total lipids have been increased in each, varying from 1,035 to 1,740 mg. per 100 cc. The total serum cholesterol has reached 335 mg. per 100 cc. in one and 375 mg. in the other. Conversion ratios in one have been 3.1 and 1.6, and in the other, 3.9 and 2.9.

Because of the spontaneous variations in size and appearance of mongrel dogs, we obtained one litter of pedigreed American bull terriers for study. Eight pups were whelped on June 12

1950, and five were given 0.99 mc. of radioactive iodine on the same day. Three of these survived one month and were given 1 mc. of radioactive iodine at this age. Only one survived the second injection. Of the three controls, one was given 5 mc. of radioactive iodine at 2 months of age. One radioactive iodine-treated dog, dying at 8 weeks, was autopsied. Sections of the thyroid revealed small islands of surviving fetal thyroid tissue. Parathyroids were identified and appeared normal grossly. E-1, the one surviving pup that had received 2 mc. of I^{131} starting at the day of birth, developed very slowly and stopped growing completely at 3 months of age (Fig. 9*B*). This animal was lethargic and lay for hours in the same position without moving. His skin was tough, dry, and redundant. His extremities, as compared with those of his litter mates, were extremely short and bowed. His abdomen was protuberant with relaxed abdominal musculature. (See Fig. 10 for appearance.) A conversion ratio done on November 10 was 11.32, or at the upper limit of hypothyroidism. After this, the serum cholesterol, 307 mg. per 100 cc. at 3 months of age, was within normal limits. The total serum lipids varied between 1,190 and 1,750 mg. per 100 cc., all increased levels.

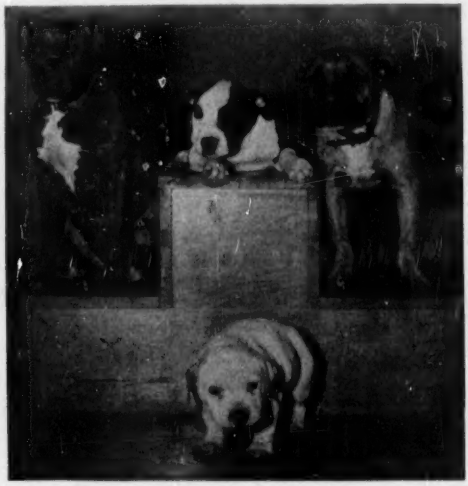

Fig. 10.—Pedigreed American bull terriers at age of 5 months. Two outside dogs are normal. The small white dog in foreground, one-third the size of the control, recevied 2 mc. of I^{131} in first month of life. The dog in the center of the platform received 5 mc. of I^{131} at 2 months of age.

E-3, the litter mate treated for the first time at 2 months of age, was the same size as the two remaining controls. He was equally active and playful at this age. After the administration of I^{131} no appreciable change was noted in his rate of development or activity for about six weeks. At this time it was noted that his rate of growth was definitely falling behind that of his normal litter mates. He was no longer as playful, and he began to be inactive in his stall. This inactivity has been progressively more marked. His hair is redundant, coarse, dry, and tough; his legs are bowed, and are considerably shortened, compared with those of his litter mates. A conversion ratio done on November 10, revealed a figure of 8.4%, a hypothyroid level. Serum cholesterols have varied from 225 to 345 mg. per 100 cc., and serum lipids have been between 1,230 and 1,815 mg. per 100 cc.

Roentgenograms were taken of this litter at the age of 8 months. In the normal dog the secondary centers of ossification for the distal radius and ulna and for the metacarpals were much better developed compared with those of the iodine-treated litter mate, E-3. The carpal bones were definitely more advanced in the control, and the pisiform bone was present in the control and not in the treated litter mate. The metacarpal bones were about one and a half

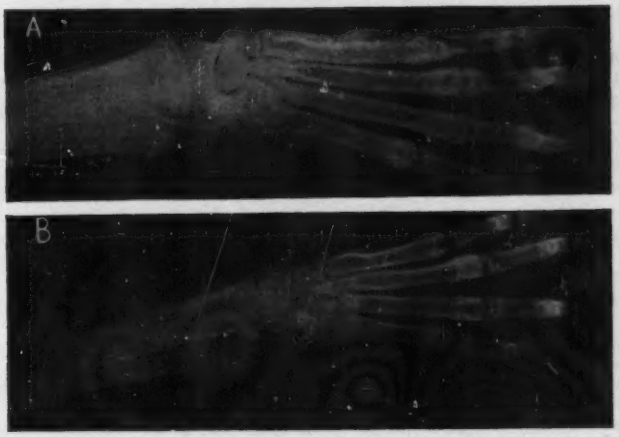

Fig. 11.—*A*, paw in normal American bull terrier, showing well-developed wrist joint and presence of pisiform bone. *B*, wrist joint in E-3, showing delayed development of all the bones and absence of pisiform bone.

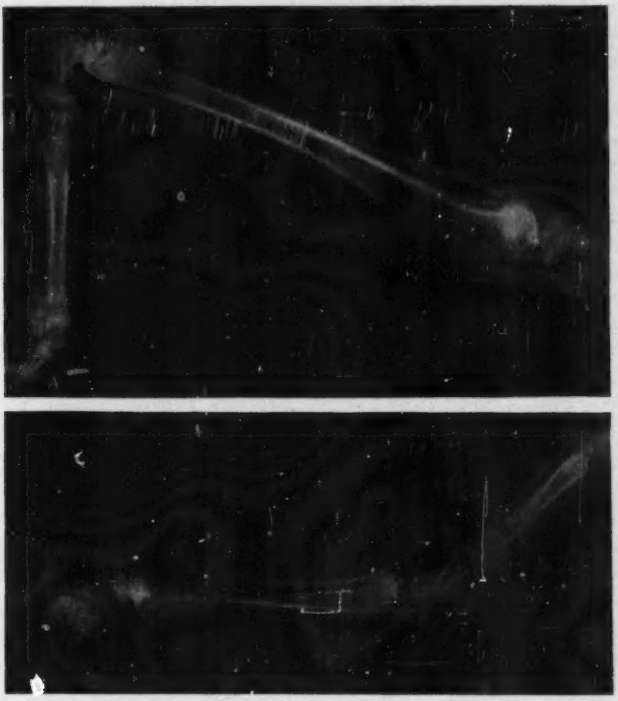

Fig. 12.—*A*, hindleg in normal American bull terrier, showing well-developed patella and epiphysis for the tibial tubercle, epiphysis for proximal tibia and distal femur. *B*, hindleg in E-3. Tibia and fibula are one-half the length of the normal, with the same width. There is delayed development of the tibial tubercle, distal femoral epiphysis, proximal tibial epiphysis, and patella. The tarsal and metatarsal bones also show delayed development.

times the length of those in the treated dog (Fig. 11). Roentgenograms of E-1, the dog treated at birth, revealed even more striking changes, although they were taken at a one month earlier age. Only five carpal bones were present, and these were very poorly developed. The metacarpal bones show an early stage of development of the distal epiphysis, and the wrist joint consists largely of cartilage. The distal epiphysis for the radius and ulna are not as yet present. Although the width of these bones is approximately normal, compared with the nontreated control, the length is markedly reduced.

E-1 died from a transfusion reaction on Jan. 2, 1951, at the age of 6 months. Sections of the thyroid revealed marked atrophy of the glandular tissue, with an increase of the fibrous stroma. No colloid was present in the glands at any point. Many vacuoles were present within the cells, indicating fatty changes in the glandular tissue. The parathyroids, although appearing grossly normal, contained a slight increase in the fibrous tissue. The hypophysis was definitely enlarged; the ovaries were immature. The adrenals, pancreas, and liver appeared grossly and microscopically normal. The head was preserved for study of the teeth, and with the animal under anesthesia, similar studies were made of E-4. The iodine-treated dog had the entire first teeth in place, with no eruption of the adult teeth. In contrast, the normal control had well-developed adult incisors, canines, bicuspids, and first molars. There appeared to have been no defect in the formation of the adult teeth in the radioactive iodine-treated animal.

COMMENT

Although experimental cretinism has been produced surgically in animals whose parathyroids are readily separable from the thyroid, similar attempts in the dog have usually failed because of the intimate connection between these two glands. Hofmeister [6] extirpated the thyroid and noticed a decreased rate of growth and a chronic undernourished state. He noted a decrease in the rate of bone growth, most marked in the long bones of the extremities, and microscopic sections revealed a decreased rate of bone formation in the epiphyseal line. In his dogs the hypophysis was increased in size, and cystic in some cases, and the ovaries were noted to be immature. Dye and Maugham [7] did thyroidectomies in three dogs of a litter of five and in two dogs of a litter of four. The thyroidectomized animals were definitely smaller, and roentgenograms revealed changes in bone formation, most marked at the epiphyseal line. They reported a retardation in the rate of growth, body weight, bone weight, and the relative level of tissue oxidation. One dog showed definite prognathia, and all had enlarged pituitaries. Binswanger [8] did complete thyroidectomies in five puppies from five different litters and compared the rate of development with that of the litter mate of similar weight and usually of the same sex. Three of the puppies were operated on between 2½ and 4 weeks, one at 7 weeks, and one at 4 months. None of the puppies operated on were dwarfed, and although there were temporary depressions in the rate of growth immediately after operation, several months after thyroidectomy there was no appreciable difference in the weight between the thyroidectomized animal and the control. The author concluded that thyroidectomy produces no marked change in the rate of either growth or development of the dog. Mayer [9] fed pure-bred

6. Hofmeister, F.: Experimentelle Untersuchungen über die Falgen des Schilddrüsenverlustes, Beitr. klin. Chir. **11**:441, 1894.

7. Dye, J. A., and Maugham, G. H.: Further Studies of Thyroid Gland, Am. J. Anat. **44**:331, 1929.

8. Binswanger, F.: Studien zur Physiologie der Schilddrüse: Schilddrüse und Wachstum (Studien am Hund), Endokrinologie **17**:22, 1936.

9. Mayer, E.: Propylthiouracil Action in Puppies, Endocrinology **40**:165, 1947.

beagles 30 mg. of propylthiouracil per kilogram of body weight from the age of 33 days to 6 to 8 months. The control and the treated dog were killed at the same age. They found no effect on the rate of growth, stature, hair, behavior, or blood. Autopsy of the normal animal revealed a small, pink thyroid with good colloid storage. In the treated animal the gland was large and purple with congested veins. Microscopic examination revealed the gland to contain unstained colloid and low to medium epithelium. The hypophysis, adrenals, pancreas, thymus, ovaries, testes, and bones were the same. The author concluded that beagles, and probably most other dogs, do not need thyroid for development.

Treatment of our dogs with radioactive iodine either in utero or post partum results in characteristic changes. The treated animals immediately grow at a slower rate, manifest by their short extremities and short body. However, they are heavier in body fat as early as several months of age. Growth curves reveal the normal animal to grow in an almost linear fashion until about one year of age, with slight change after this except for deposition of fat. The iodine-treated animals show two characteristic types of growth. In one type, the animal grows in a relatively linear fashion but at a slower rate than the control, until 6 to 8 months of age. The weight levels off for 3 to 6 months, and then has a second sharp rate of increase at about one year, as the animal becomes fat. In the other type of growth the rate of increase in weight begins to fall at 3 to 4 months, and the weight increases slowly until about one year and then stops.

The dog has the same bone changes in cretinism as has been reported in other animals. The defect in development is one of endochondral ossification. The width of the shaft of the long bones is normal, but the length is decreased because of delayed appearance and poor development of the secondary centers of ossification, as well as disorderly and impaired laying down of osteoid and bone at the epiphyseal lines. The dog also has delayed closure of the epiphyseal lines. In our limited studies on one litter we have noted a delayed appearance of the second dentition.

Changes in the other endocrines have been noted. As previously reported by Hofmeister [9] and by Jeandelize,[10] the ovaries and testes were immature. We have also noted an increased size in the hypophysis following destruction of the thyroid, previously reported in rabbits by Rogowitsch.[11] We have not found the cystic changes described by Hofmeister.[9] However, we have seen in two dogs pronounced prognathia, similar to that seen in acromegaly. We have noted no changes in the pancreas or adrenals.

The appearance of the thyroid gland itself varied. In dogs who had received I^{131} 10 days to three weeks prior to death some remnant of thyroid could be found. It consisted mainly of areolar tissue with occasional islands of fetal thyroid. No colloid was seen in any specimen. After five weeks, either no remnant or a remnant consisting only of areolar tissue was found, except in E-1, described above. The parathyroids appeared to be not at all damaged grossly and showed only a minor increase in fibrous tissue microscopically. Serum calcium determinations when done showed normal values.

10. Jeandelize, P.: Insuffisance thyroidieme at parathyroidieme, Thesis, Nancy, 1902.

11. Rogowitsch, N.: Die Veränderungen der Hypophyse nach Entfernung der Schilddrüse, Beitr. path. Anat. **4**:453, 1888.

We also have chemical evidence of destruction of the thyroid. The typical increase of total serum cholesterol and total serum lipids was always present. When tracer doses of I^{131} were given, no localization in the neck occurred. The ratio of free to protein-bound iodine fell within the hypothyroid level in all instances.

These dogs also showed other common physical changes. Their skin was coarse, thickened, dry, scaly, and tough. The hair was coarse, dry, and brittle. Usually these animals were lethargic and lay for hours without moving, although several occasionally did play together. Two dogs showed protruding tongues.

In the litters treated with I^{131} in utero, the changes were more profound. Such instinctive functions as nursing and moving toward the mother were absent. The mortality rate has been very high, only one of eight and three of seven surviving in the litters treated 10 days before birth. These animals have been only one-fourth to one-half the size of their mother.

SUMMARY AND CONCLUSIONS

Experimental cretinism may be produced in dogs by administration of I^{131} to the pregnant bitch prior to whelping or to the newborn dog during the first few months of life.

Cretinism in dogs is characterized by impairment of growth and skeletal development, obesity, lethargy, coarse, dry skin and hair, and, occasionally, protuberant tongues.

Cretin dogs have hyperlipemia and hypercholesteremia, and conversion of free to protein-bound iodine is depressed.

Associated endocrine changes are the immaturity of the gonads and increase in size of the pituitary.

DIRECT MEASUREMENT OF INTRAVASCULAR PRESSURE IN COMPONENTS OF THE CIRCLE OF WILLIS

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CONTINUED interest in the neurosurgical treatment of congenital cerebral aneurysms of the circle of Willis and of vascular anomalies of the brain has stimulated an objective analysis of many aspects of the physiology of the cerebral circulation. Of these, an accurate evaluation of the adequacy of cross circulation in the circle of Willis is of primary importance to the neurosurgeon. There is abundant clinical evidence to show that disastrous tissue anoxia may ensue after ligation of the internal carotid artery in the neck or clip ligation of this same vessel within the cranium, if blood flow resistance across the circle of Willis is high.

The Matas test, initiated by digital compression of the internal carotid artery in the neck, customarily indicates gross inadequacies in hemispheral cross circulation, but a normal reaction to the Matas test does not guarantee freedom from cerebral complication secondary to anoxia. The concomitant use of an electroencephalogram and digital compression of the internal carotid artery has also failed to disclose such borderline instances of inadequate cross circulation. Sweet and Bennett [1] and Sweet, Sarnoff and Bakay [2] have recorded accurate measurements of the intravascular pressure within the carotid artery in the neck when this vessel was occluded proximally. The average of observations on 26 adults showed that occlusion of the internal carotid artery in the neck caused a drop in systolic pressure to 51%, in pulse pressure to 31% and in the integrated mean pressure to 57% of the original levels. When pressure falls to 30% of the original level were encountered, as they were in three patients, inadequate cross circulation was proved by the onset of complications in two of these patients after neck ligation. Confirmatory

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1. Sweet, W. H., and Bennett, H. S.: Changes in Internal Carotid Pressure During Carotid and Jugular Occlusion and Their Clinical Significance, J. Neurosurg. **5**:178-195, 1948.

2. Sweet, W. H.; Sarnoff, S. J., and Bakay, L.: A Clinical Method for Recording Internal Carotid Pressure (Significance of Changes During Carotid Occlusion), Surg., Gynec. & Obst. **90**:327-334, 1950.

results have been published by Brackett and Mount,[3] using the technique of indwelling carotid artery catheters. Both groups of observers have pointed out the marked variations in these objective measurements from case to case and have emphasized the importance of individual study of patients prior to the application of any standard form of therapy.

Because of the technical requirements of the apparatus and the neurosurgical problem that may be encountered in individual patients, few opportunities have presented themselves for an extension of this analysis of intravascular pressure to components of the circle of Willis. In four patients, one with congenital cerebral aneurysm, and three with arteriovenous anomalies, direct measurements of the intravascular pressure within the intracranial internal carotid artery, the middle cerebral artery and the end vessels of the aneurysms have been recorded.

METHOD

All pressures were obtained with a Sanborn electromanometer through a No. 27 gauge needle 6 cm. in length and recorded with a Sanborn direct current amplifier-

TABLE 1.—*Arteriovenous Aneurysm of Right Temporal Lobe in Case 1*

Pressure in Common Carotid (Mm./Water)			Pressure in Internal Carotid			Pressure in Internal Carotid (Intracranial)			Pressure in Middle Cerebral		
	Proximal Occlusion	% Drop		Proximal Occlusion	% Drop		Occlusion, Common Carotid (Neck)	% Drop		Occlusion, Common Carotid	% Drop
106	64	43%	104	80	23%	104	60	42%	100	60	40%
							Occlusion, Internal Carotid (Neck)	% Drop		Occlusion, Internal Carotid (Neck)	% Drop
						104	64	37%	100	68	32%

recorder. Patients were selected for this study who had vascular lesions in the nondominant hemisphere, and further selection was dictated by safety factors after visualization of the lesion. The common, external and internal carotid arteries were exposed in the neck, followed by craniotomy and exposure of the vascular disorder. In Case 2, the aneurysm began to bleed at the moment of exposure and the right anterior cerebral artery was clipped before intravascular pressure readings were recorded.

Pressure measurements were taken in sequence from the proximal portion of the arterial tree to the most distal arterial segment. After withdrawal of the needle, minimal bleeding from the intracerebral vessels was controlled by the pressure of a gelatin foam pledget. None of the patients showed untoward sequelae. Since apparatus for the continuous flushing of the recording system is not generally available, moderate damping effects were noted. This could be obviated by intermittent flushing and by comparison of pressures at similar time intervals thereafter. The figures presented represent the systolic pressures before and after occlusion.

3. Brackett, C. E., and Mount, L. A.: Some Observations of Intracarotid Blood Pressure Made During Carotid Ligation for Intracranial Aneurysms, in Surgical Forum, Philadelphia, W. B. Saunders Company, 1950, pp. 344-350.

TABLE 2.—*Congenital Cerebral Aneurysm of Left Anterior Cerebral and Anterior Communicating Arteries in Case 2*

Pressure in Internal Carotid (Neck)			Pressure in Internal Carotid (Intracranial)			Pressure in Middle Cerebral		
	Occlusion, Common Carotid	% Drop		Occlusion, Internal Carotid	% Drop		Occlusion, Internal Carotid	% Drop
132	88	30%	126	96	24%	132	112	15%
	Occlusion, Internal Carotid	% Drop						
132	94	28%						

TABLE 3.—*Arteriovenous Aneurysm of Right Parietal Lobe in Case 3*

Pressure in Internal Carotid (Neck)			Pressure in Anomaly		
	Occlusion, Common Carotid	% Drop		Occlusion, Common Carotid	% Drop
100	56	44%	80	48	40%
	Occlusion, Internal Carotid	% Drop		Occlusion, Internal Carotid (Neck)	% Drop
112	56	50%	80	48	40%
				Occlusion, Feeder	%
			80	56	30%

TABLE 4.—*Arteriovenous Aneurysm of External Carotid Artery-Petrosal Sinus in Case 4*

Pressure in Anomaly		
	Occlusion, Common Carotid	% Drop
76	25	67%
	Occlusion, External Carotid	% Drop
76	18	76%

COMMENT

This preliminary effort to record intravascular pressures in the major arteries of the brain and in the abnormal vascular channels of arteriovenous anomalies demonstrates the inherent safety and value of this technical procedure. With improvement in apparatus, there appears to be no valid reason why intravascular pressure cannot be obtained from all components of the cerebral circulation available for testing. The effect of damping is that of decreasing the systolic pressure and elevating the diastolic pressure, so that the mean pressure is approached. With this reservation, the comparative pressure readings seem valid.

Individual variations in intravascular pressure are apparent even in this small series of cases, but there appears to be a constant fall in arterial pressure along the entire vascular segment after occlusion. Whether this fall in pressure remains constant when vascular channels effecting cross circulation are impaired by pathological changes or by operative ligation remains to be proved. This study and those that have been noted suggest strongly that this method of intravascular recording of hemispheral cross circulation will prove a valuable adjunct to the neurosurgical control of these lesions.

TOCOPHEROLS IN TREATMENT OF PRIMARY FIBROSITIS

Including Dupuytren's Contracture, Periarthritis of the Shoulders, and Peyronie's Disease

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CONTINUED observations over the past decade of the clinical value of the tocopherols (vitamin E) in the treatment of primary fibrositis have yielded sufficient promising results to warrant a review at the present time. Thomson,[1] in commenting on this subject, wrote the following sentence: "In fact, the general response has been so good that to assert that vitamin E has a specific effect on Dupuytren's contracture does not appear to be unduly reckless."

The results reported by Thomson concerned cases of Dupuytren's contracture involving 22 hands that were treated with vitamin E. All patients except one were treated with ephynal, 4 (50 mg.) tablets being the daily dose. The duration of the period of treatment varied from 12 to 20 weeks. The majority were treated for 20 weeks. He divided the severity of the Dupuytren contracture into Groups A, B, and C. Group A consisted of the early cases in which the palmar bands were present to a moderate degree and the fingers were not contracted closer than 90 degrees toward the palm. Group B consisted of the late or chronic cases in which thickening of the palmar fascia was gross and the affected fingers were fixed in the palm. Group C included old cases in which operation had been performed, with recurrence. The 10 patients in Group A had a clinical response varying from some absorption of the palmar fibrosis to complete cure of the condition. Full extension of the fingers was obtained in five cases. Marked improvement suggesting that complete extension would eventually be obtained was present in three cases. No contractures were present in the other two cases in this group, and absorption of the palmar fibrosis occurred with treatment. Eight patients were treated in Group B, which included the late or chronic cases. The palmar fibrosis softened in all these cases. Also, there was increased movement of the fingers as a result of treatment. Four of these cases came to surgery, and the results were excellent in three instances and only fair in one instance. Vitamin E therapy in Group C halted the process of recurrence in all four patients treated. Extension was regained in two cases. Scardino and Scott[2] discussed six cases in which 300 mg. of mixed tocopherols or 200 mg. of ephynal daily was used for treatment. One patient showed marked improvement and three moderate improvement, and failure occurred in the two other cases. Personal com-

This study has been aided by a Grant from the Squibb Institute of Medical Research.

Dr. Steinberg is Director of the Arthritis Clinic, Associate Chief of Medicine, Rochester General Hospital.

1. Thomson, G. R.: Treatment of Dupuytren's Contracture with Vitamin E, Brit. M. J. **2**:1382, 1949.

2. Scardino, P. L., and Scott, W. W.: Use of Tocopherols in the Treatment of Peyronie's Disease, Ann. New York Acad. Sc. **52**:390, 1949.

munications from many physicians during the past decade add credence to Thomson's opinion given in the opening paragraph of this report.

It is interesting that even the defenders of the opinion that vitamin E may have some value in the treatment of Dupuytren's contracture and other fibroblastic diseases present oblique confirmation of this fact. Parsons [3] treated one patient with Dupuytren's contracture with 300 mg. of ephynal in three equally divided doses daily for a period of 100 days. (The patient thought he could move the ring finger a little more freely, but objectively there was no definite change in the contracture or in the skin of the palms.) During the first 17 days of the 100 day treatment the patient received variable amounts of ephynal ranging from 60 to 80 mg. three times daily. King [4] originally reported the clinical results in 13 patients treated with 300 mg. of ephynal daily for a period ranging up to eight weeks. He stated that further treatment was impossible in four cases because of toxic manifestations. (No such toxic manifestations had been found in thousands of patients who have received vitamin E for this and other conditions.) Other patients were "sure they had gained improvement, but none was seen."

MODUS OPERANDI

Both the blood vitamin E level and the vitamin E tolerance curve have been found normal in persons with primary fibrositis.[5] The only exception is in cases in which there is concomitant existence of portal cirrhosis, when an abnormally low vitamin E level and a plateau curve is obtained. Recent studies in other fields have demonstrated amply that both hormones and vitamins in large doses may act as pharmacological agents rather than replacement agents of a deficiency condition. Decrease in the size and lessening of the number of fibroblasts [6] have been shown to occur with the pharmacological use of corticotropin (ACTH) and cortisone. We may repeat, with Thomson, that it does not appear unduly reckless to believe that similar action may occur with tocopherols. Objective evidence to support this contention is found in the change in the skin of the palm of the hand from a puckered leathery skin to a smooth soft one. The puckering and changes in the skin in Dupuytren's contracture are caused by the fibroblastic activity. Hence, a reversion to normal of the skin texture must be due to a change in the fibroblasts.

DUPUYTREN'S CONTRACTURE

Beneficial effects from the tocopherols in the treatment of Dupuytren's contracture are as follows: (*a*) reversion of the sclerodermic palmar skin to a soft normal texture in all patients treated; (*b*) cessation of the process of fibrosis in all cases; this assertion is made after periods of a two to 10-year follow-up obser-

3. Parsons, A. R.: Dupuytren's Contracture: Treatment by Massive Doses of Vitamin E. Irish J. M. Sc. **272**:274, 1948.

4. King, R. A.: Vitamin E Therapy in Dupuytren's Contracture: Examination of Claim That Vitamin Therapy is Successful, J. Bone & Joint Surg. **31**:443, 1949.

5. Steinberg, C. L.: New Method of Treatment of Dupuytren's Contracture: A Form of Fibrositis, M. Clin. North America **30**:221, 1946. Klatskin, G., and Krehl, W. A.: The Significance of the Plasma Tocopherol Concentration and of Tocopherol Tolerance Tests in Liver Disease, Jr. Clin. Invest. **29**:1528, 1950.

6. Ragan, C.; Grokoest, A. W., and Boots, R. H.: Effect of Adrenocorticotrophic Hormone (ACTH) on Rheumatoid Arthritis, Am. J. M. **7**:741, 1949.

vation; (*c*) marked to complete reversion to normal of palmar fibrosis in Grade 1 and Grade 2 cases, and (*d*) marked to complete improvement of symptoms of primary fibrositis present elsewhere (such as recurrent lumbago, Peyronie's disease, recurrent torticollis) often associated with Dupuytren's contracture.

This report on Dupuytren's contracture concerns 22 cases not previously reported. Various criteria are set up in this paper in order to evaluate critically the clinical value of vitamin E.

Dupuytren's Contracture

Case	Age	Sex	Duration	Grade	Occupation	Cure	Improved	Failure	Treatment *
1	54	M	7 yr.	1	Salesman	+	..	..	2 mo., F
2	69	M	?	2	Merchant	..	..	+	4 mo., R 6 mo., F
3	59	M	11 yr.	2	Watchman	..	+	..	2 yr., R 17 mo., F
4	60	F	?	1	Saleswoman	..	+	..	2 mo., R 2 mo., F
5	27	F	3 mo.	2	Housewife	+	..	..	4 mo., R
6	72	F	10 yr.	3	Housewife	..	..	+	10 mo., F
7	65	F	25 yr., lumbago; 12 yr., Dupuytren's	3	Physician	..	..	+ (Lumbago cured)	4 yr., F
8	73	M	10 yr., Dupuytren's; 5 yr., shoulder	2	Railroad engineer	..	+ shoulder well	..	15 mo., R
9	29	M	10 yr.	4 (Also soles of feet)	Physician	..	..	+	2 mo., R
10	63	F	10 yr.	2	Housewife	+	..	..	6 mo., R
11	64	F	3 yr.	3	Housewife	+	..	..	2 yr., R
12	59	F	4 yr.	2	Laborer	..	+	..	3 yr., R
13	60	M	6 yr.	3	Contractor	..	..	+	1 yr., F
14	45	M	10 yr.	4	Importer	..	..	+	9 mo., R
15	60	F	?	1	Housewife	+	..	..	5 mo., R
16	52	F	18 mo.	1	Teacher	+	..	..	4 mo., R
17	56	M	12 yr., right hand 5 yr., left hand	4	Diplomat	..	+	..	4 mo., R
18	51	M	3½ yr.	2	Salesman	+	..	..	3 mo., R
19	60	F	3 yr.	1	Housewife	..	+	..	2 mo., F
20	40	M	8 yr.	3	Chemist	..	..	+ skin softer (Surgery easy)	3 mo., F
21	57	M	2 yr.	1	Salesman	+	..	..	7 mo., R
22	55	M	5 yr.	3	Laborer	+	..	..	3 mo., F

* F indicates fortified and R, regular tocopherols.

CLASSIFICATION OF DUPUYTREN'S CONTRACTURE

Dupuytren's contracture may be classified under the following grades: grade 1, fibrosis of palmar fascia without contractures; grade 2, contractures up to 135 degrees toward the palm; grade 3, contractures up to 90 degrees toward the palm, and grade 4, fibrosis of palmar fascia, with flexion deformities of the fingers beyond 90 degrees toward the palm, and marked "valleys" between the contracting bands.

This series of 22 cases of Dupuytren's contracture included 12 men and 10 women. The mean age of the men was 54 years and that of the women 58.2 years. A trend but no conclusive evidence may be noted from this small series of cases. The trend indicates that sex in itself has very little bearing on the etiology of this

condition. Also, the mean age in the two sexes is almost equal. An analysis of the effectiveness of tocopherols in the various grades of Dupuytren's contracture gave the following data: Of six patients with grade 1, five obtained a cure and one improved; there were no instances of complete failure. Of seven patients with grade 2, three were cured, three showed clinical improvement and in one the result was a failure. Among six patients with grade 3, there were two cures and four failures. Of three patients listed with grade 4, none of whom was cured, one showed clinical improvement and in two the treatment failed. One of the patients in whom the treatment failed was subsequently operated on. The operation was easy, and the clinical result was excellent.

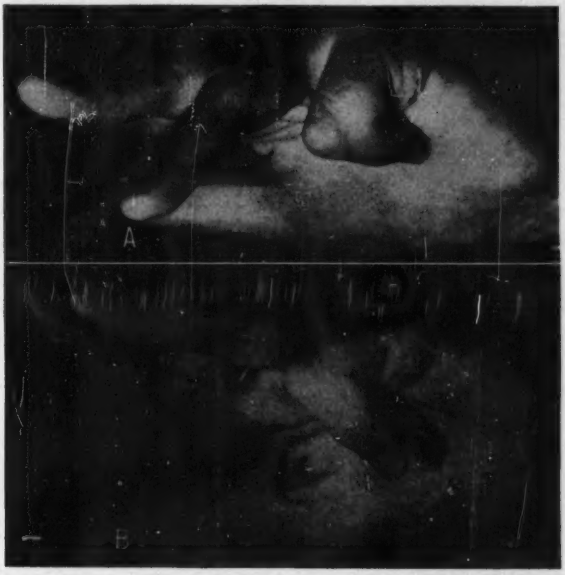

Fig. 1.—Hand of H. B., 56-year-old diplomat, with 12-year history of Dupuytren's contracture, grade 4. *A*, before treatment; *B*, after four months' treatment with regular tocopherex.* Note sufficient improvement in little finger to accommodate handle of brief case.

Sufficient clinical history was obtained in 18 patients to determine the duration of the Dupuytren contracture. A cure was obtained in one patient who had suffered from the condition less than one year. Five patients were cured and two showed improvement under this mode of therapy in the group of patients having Dupuytren's contracture over a one- to five-year period. There were two cures, four instances of clinical improvement, and five failures in the group who had the condition for more than five years. The prognosis is better in patients in whom the disease has been of shorter duration and less severe. Only two of the 22 patients followed a hazardous occupation (laborers). This fact indicates that trauma is not an important factor. Pictorial changes of some representative cases are described.

Case 1 (H. B.).—The small finger of the right hand was "plastered" against the palm of the hand. The flexor tendon of the third, fourth, and fifth right fingers was markedly involved by thick fibrous tissue. Four months' treatment with 300 mg. daily doses of mixed natural tocopherols resulted in marked clinical improvement, seen in Figure 1*B*.

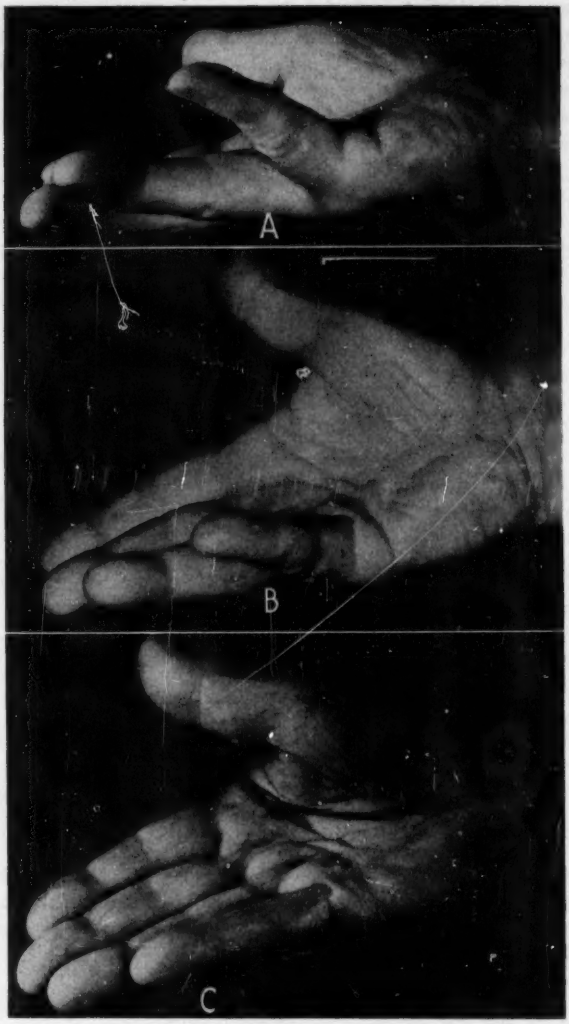

Fig. 2.—Hand of A. McN., 63-year-old white woman, with 10-year history of Dupuytren's contracture. *A*, before treatment; *B*, after four weeks with regular tocopherex®; *C*, at the completion of six months' treatment with regular tocopherex.®

Case 2 (A. McN.).—A 63-year-old white charwoman had decided on surgical treatment. She was advised to try tocopherol therapy first and if this failed to undergo surgery. Marked clinical

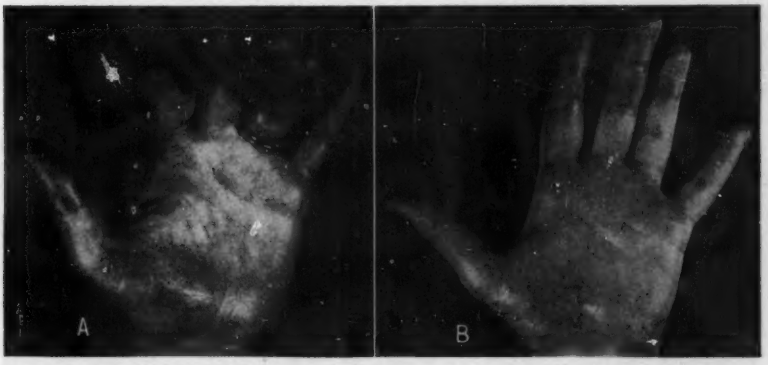

Fig. 3.—Hand of B. C., a housewife aged 27. *A*, history of three months' Duyuytren's contracture before treatment; *B*, after three months' treatment with regular tocopherex,● complete cure.

Fig. 4.—Hands of K. A., a 51-year-old salesman, with a history of Dupuytren's contracture for three and a half years. *A*, before treatment; *B*, after three months' treatment with regular tocopherex,● complete cure.

improvement is noted over the six month period in which 300 mg. of mixed natural tocopherols was taken daily. Marked "giving" of the fibrous band is noted in the serial photographs.

CASE 3 (B. C.).—This was not the usual picture of marked fibrosis involving one or several flexor palm tendons. A diffuse sclerodermatous texture with secondary contracture was noted in

Fig. 5.—Hand of J. B. aged 59, with Grade 1 Dupuytren's contracture. *A*, change before tocopherol therapy; *B*, palm of hand after two years' treatment with regular tocopherex® and 17 months' treatment with fortified tocopherex.®

Fig. 6.—Hand of J. B., a 45-year-old importer with a 10-year history of Dupuytren's contracture. Complete failure after nine months' treatment with regular tocopherex.® This is the type of case that requires surgery.

all the digits. The patient has been observed now for eight years. If minimal amounts, 50 mg. daily, of mixed natural tocopherols are not taken, a gradual return of the condition ensues in a period of two to three months.

CASE 4 (K. A.).—The patient consumed large quantities of alcohol over a period of years. No doubt his nutritional status must have been poor during his worst bouts. Unfortunately, the blood vitamin E level was not determined until he had been getting 300 mg. of mixed natural tocopherols for two weeks. It was then normal at 1.09 mg. per 100 cc. Under this same therapy the blood vitamin E level rose to 1.33 mg. per 100 cc. in four more weeks and was 1.31 mg. two weeks later.

CASE 5 (J. B.).—A 59-year-old night watchman has been observed for seven years. He requires 150 mg. of mixed natural tocopherols daily to prevent progression of fibrosis in the palms. No marked change was noted when the dose was changed from 300 mg. of mixed natural tocopherols to 400 mg. of fortified mixed natural tocopherols.

CASE 6 (J. B.).—This type of case, with marked "valleys" between the fibrosed flexor tendons, requires surgery. Tocopherol therapy alone fails.

PERIARTHRITIS OF THE SHOULDERS

Duplay's syndrome, frozen shoulders or periarthritis of the shoulders, is an intriguing condition. Sutro and Cohen's [7] article on the painful shoulder published 10 years ago generally upheld the metabolic versus the traumatic theory as the cause of calcification of tendinocapsular tissues particularly involving the shoulder joint. They found that 50 to 100 mg. of alpha tocopherol acetate per day would bring improvement in acute cases in three days and complete subsidence of pain within seven to 21 days. Smaller doses, 5 to 20 mg., relieved pain in two to 20 days. The latter change is not noteworthy since the same pattern will result if placebos are given. Alvin Barach, in a recent personal communication, wrote of his excellent results of treating acute subacromial bursitis with parenteral alpha tocopherol. About 10 years ago, I treated 21 patients with primary fibrositis with 100 to 300 mg. of alpha tocopherol intramuscularly at weekly intervals. Oleogranulomas developed in seven patients nine to 12 months after the last injection. These cases presented painful swollen large areas measuring 3 to 5 cm. at the site of injection. These areas were excised in two patients. The typical microscopic picture is shown in both low-power and high-power photomicrographs (Fig. 7). The miscroscopic picture shows many foamy cells in a granulomatous stroma. The material within the cells stained faintly acid. No acid-fast bacilli were present. The diagnosis was oleogranuloma. These oleogranulomas have disappeared spontaneously in a period of two to three years in the other five cases.

The shoulder syndrome is common to various conditions. Thus, it is not uncommon to note a very painful shoulder with limitation in abduction and internal rotaton in patients who have a positive calcium x-ray shadow demonstrated in the subacromial bursa. These patients suffer acute episodes of severe pain. Also, it is not uncommon for persons with generalized rheumatoid arthritis to have painful stiff shoulders. On occasion direct trauma to the shoulder joint produces an acute inflamed subacromial bursitis. At times, an acute painful shoulder is associated with gout. More often patients have painful stiff shoulders unassociated with the previous conditions, Sutro and Cohen.[7] Roentgenograms of the shoulder are negative. Chemical data on the blood are normal; the sedimentation rate is normal, and no positive calcium shadow is obtained on the roentgenogram. Six patients were treated successfully with the fortified preparation of the tocopherols. Three were women and three were men. The period of the duration of the condition varied from

7. Sutro, C. J., and Cohen, L. J.: Basis and Treatment of Calcification of Tendinocapsular Tissues, Especially Supraspinatus Tendon, Arch. Surg. **42**:1065, 1941.

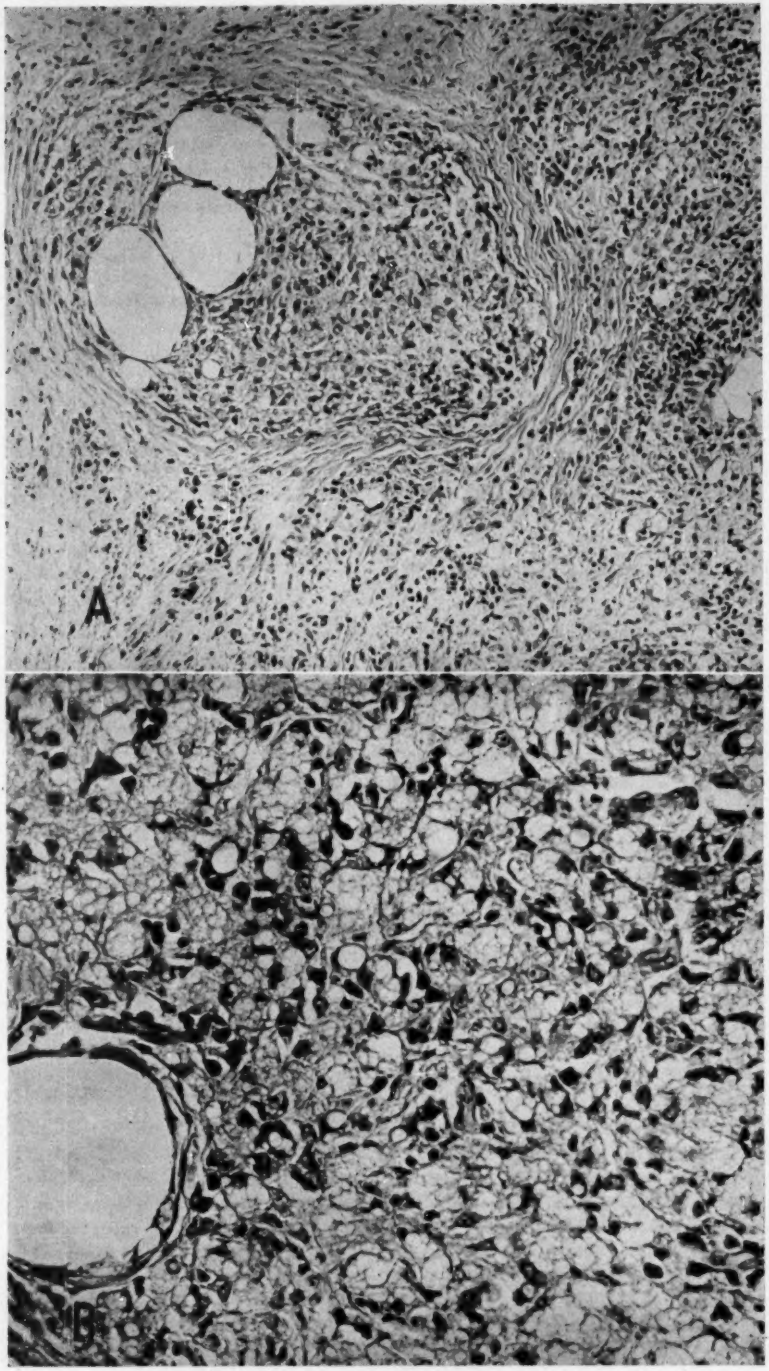

Fig. 7.—*A*, low-power photomicrograph of oleogranuloma removed one year after patient received alpha tocopherol intramuscularly; × 180. *B*, high-power photomicrograph in same case showing many foamy cells in a granulomatous stroma; × 300.

two weeks to three years. The shortest period required to obtain complete cure of the condition was two weeks, and the longest period of treatment was two months. Also, 12 patients with frozen shoulders were treated for a period ranging from three to 12 months without clinical benefit.

PEYRONIE'S DISEASE

Three patients with this condition were treated with the fortified preparation of the tocopherols. A young man aged 35 obtained complete cure of this condition in two months. One patient was treated for 14 months and was able to have an erection without deformity of the organ. Another patient, aged 62, had slight improvement in that the deformity on erection was slight but was still present at the end of 15 months of therapy.

Three patients who suffered from recurrent lumbago, with normal sedimentation rates and minimal to no osteoarthritis of the vertebral column, were treated with the regular preparation of tocopherols, and all three were completely relieved of their symptoms.

SUMMARY

Twenty-two patients with Dupuytren's contracture, 18 patients with Duplay's syndrome, three patients with Peyronie's disease, and three patients with lumbago were treated with mixed natural tocopherols. Sufficient clinical improvement was obtained to warrant this therapy. A hypothesis is described which may explain the therapeutic effectiveness of the tocopherols in these conditions. This study does not indicate the superiority of fortified tocopherols as compared to the regular mixed natural tocopherols.

USE OF SKELETAL TRACTION FOR MASS TREATMENT OF COMPOUND FRACTURES

A Summary of Experiences with 4,290 Cases During World War II

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THERE are practical considerations and technical details about the use of skeletal traction in war fractures which need not be learned by costly experience. In view of the present international situation, the techniques of management of multiple fractures may be reviewed with profit by civilian as well as military medical personnel. The experience with fractures at the onset of the second world war in relation to the first world war emphasized the wisdom of George Santayana's remark that "those who do not know history are doomed to repeat it."

In World War II, shortly after the North African Campaign, surgeons in general and station hospitals of the European Theater of Operations were instructed by circular letters and directives from the Theater Surgeon to treat fractures of the long bones wherever possible by skeletal traction and balanced suspension. These instructions, which originated from World War II experience rather than civilian trends in surgery, determined the treatment of approximately 1,200 battle casualties evacuated to the Southern Base Station, United Kingdom, between June 6, 1944, and May 8, 1945. Thus, the value of skeletal traction in patients with extensive war wounds, although fully appreciated at the conclusion of World War I, had been rediscovered just in time in World War II.

This paper is a summary of experience with the use of skeletal traction in 4,920 patients treated by us at the 802d Hospital Center and described in detail in a historical report to the Chief Consultant in Orthopedic Surgery, European Theater of Operations, May 15, 1945.

The immediate results and follow-up reports from observers in army hospitals in the United States substantiated Cleveland's recent statement that "skeletal traction is the safest and simplest method of mass treatment of compound fractures of the long bones." [1] During World War II the method was quickly mastered by

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1. Cleveland, M.: Emergency Treatment of Bone and Joint Casualties, J. Bone & Joint Surg. **32**:235-248, 1950.

general physicians, obstetricians, pediatricians, and others who had no previous experience with fractures and who were assigned to surgical services in an emergency or in shortages of trained personnel in overseas hospitals.

FRACTURES ASSOCIATED WITH EXTENSIVE BURNS

A statistical study of the atomic bomb casualties at Hiroshima and Nagasaki in Japan has aroused great interest in the problem of simultaneous compound fractures and burns. Approximately 15 cases of severe burns of one or two limbs with compound fractures were observed from Armored Corps battle casualties in which the men were unable to get out of the vehicles in time to save themselves from gasoline fires. In all instances, the patients were transported by air ambulance in plaster casts, administered plasma, blood, and antibiotics and immediately suspended in traction on their arrival in the United Kingdom. Split-thickness skin grafts were usually applied to the burned areas within three to four weeks. The reaction of burned skin and underlying bone to perforation by a Kirschner wire was not determined. In every patient treated by us, the burned area was deliberately avoided and a compromise was made in the treatment of the fracture by the insertion of the wire at a point distal to the site of election. Current views of this important point may be summarized as follows:

1. "Putting wires through burned skin involves a virtual certainty that the pin tract would become infected with gram-positive cocci that are resistant to penicillin after about the eighteenth day of treatment."[1a]

2. If such bone tract infections ensue, they may be of no long-term significance. The wire may be inserted through burned skin or granulating wounds in instances in which the entire limb is involved and there is no alternative.

GENERAL CONSIDERATIONS

Battle-incurred compound fractures were associated with extensive damage to soft parts and usually did not follow the standard patterns of closed injuries. Each case required its own analysis, with careful consideration of such factors as the extent of destroyed or paralyzed muscle, the position and size of the wound or wounds, and the need for ready accessibility of the limb for wound closure, skin grafts, and nerve suture. Only rarely could traction alone be depended on to effect satisfactory reduction. Carefully planned gentle manipulation was almost always necessary to reduce the fractures. Intravenous thiopental sodium anesthesia supplemented by oxygen and nitrous oxide was the one of choice and was well tolerated by healthy young soldiers with multiple injuries. The exploration, wound closure, and suspension of the fractures required several hours and had to be considered a major operation. This demanded preoperative and postoperative attention to blood replacement, fluid balance, antibiotics therapy and dietary supplements.

The Kirschner wire was used almost exclusively for skeletal traction. Although in many instances the greater surface area of the heavier Steinmann pin might theoretically have been an advantage, the wire was tolerated better. One of the most important lessons learned was that the wire must be inserted with the limb in its final position in traction. If, for example, a wire is inserted transversely in the

1a. Moore, F.: Personal communication to the authors.

supracondylar area of the femur with the leg in extension and the knee is then flexed, the skin and the subcutaneous soft tissues will be folded against or stretched around the wire and within a few days an infected conical cavity extending down to bone will develop. This does not mean that the wire could not be inserted and then used as a handle for manipulation. However, when this was done the limb was placed in its final position, the wire was inserted, and the manipulation then carried out. The wire was inserted whenever possible at right angles to the long axis of the bone. Skin was punctured directly by the wire itself and on the opposite side it was allowed to create its own aperture. Pin sepsis, loosening, drifting, and even ring sequestra appeared, but far less often than might have been expected. In no instance did these complications produce chronic osteomyelitis. Because of the normal process of bone resorption, even perfectly inserted wires became loose seven to eight weeks after insertion. Using whatever was most available, individual surgeons employed blocks of sterile felt, corks, or sponge rubber between the skin and the tautening bow to prevent sliding of the wire. Wires were never inserted into bare bone or through wounds. It was almost always possible to find a compromise arrangement of the skeletal traction and use adjacent areas with uninjured normal skin and bone. The amount of weight required to maintain reduction was on the whole much less than had been anticipated from experience with common civilian accidental fractures because of the large volume of destroyed or paralyzed muscle. When this was realized, distraction was avoided.

The general principles of the care of battle casualties and injuries involving bones and joints has recently been outlined by Cleveland, Manning, and Stewart [2] in the "Manual of Therapy of the European Theatre of Operations." The reader is referred to elementary textbooks of surgery for sketches and instructions for the standard arrangements for suspension of fractures in a Balkan frame. The discussion here will be limited to fundamental principles of treatment of extensive war fractures by skeletal traction.

1. THE HUMERUS

One thousand sixty-five compound fractures of the humerus were treated in skeletal traction. These fell into three groups:

A. The Upper Third.—Traction through the olecranon process was used in all but a few of this group. The Kirschner wire was introduced from the medial to the lateral side. The ulnar nerve was identified by palpation and carefully avoided. In no case was there permanent nerve damage, but in a few instances a temporary neuritis developed from irritation by the adjacent pin. The humerus was, as a rule, held at right angles to the thorax and in midrotation (Fig. 1). Often it was necessary to keep a posterior wound from contact with the underlying bed or apparatus. In some cases, the axis of the immobilization apparatus was applied with the humerus at anterior flexion 90 degrees and the traction was directed overhead.

The "hanging cast" was found to be unsuitable for early treatment of extensive fractures with open wounds. After a good callus had developed at six to eight weeks, a thoracobrachial or "hanging" type plaster could be substituted for traction.

2. Cleveland, M.; Manning, J., and Stewart, W. J.: Care of Battle Casualties and Injuries Involving Bones and Joints, J. Bone & Joint Surg. **33**:517-540, 1951.

B. The Middle Third.—Traction through the olecranon was also found most satisfactory for this group of cases. Approximately 20% of the cases in this group exhibited radial nerve weakness or paralysis in which recovery occurred sometimes as early as 72 hours after reduction and institution of traction. Fractures of the

Fig. 1.—Skeletal traction applied for treatment of 88 mm. shell fragment, wounds including compound comminuted fractures of the radius and ulna and simple fracture of the humerus incurred in combat in France in 1945.

humerus were rarely manipulated and were often reduced by traction alone. Ten pounds of weight for 12 to 24 hours almost invariably produced satisfactory alignment. Weight was then usually reduced to four to six pounds. The Thomas arm splint was used only when a Pearson attachment was needed for traction on the forearm (Fig. 1). Complete interruption of the radial nerve and loss of bone sub-

stance were frequent complications. Deliberate shortening of the humerus was advocated to facilitate suture of the nerve but not until the wounds were clean and covered with good skin. The presence of infection and the loss of muscle, vascular, and nerve tissue directly over the fracture site were a direct threat to the function of the hand and were obviously more important than strict immobilization and purely mechanical treatment of fractures of the arm or forearm.

C. The Lower Third and Elbow.—Early motion of the elbow joint and hand was the primary consideration in this group, and anatomical reposition of fragments was not sought at the price of immobilization. Traction was instituted either through the olecranon process or at some point in the dorsal cortex of the proximal third of the ulna. Active motion of the hand in the traction apparatus was begun at the earliest possible moment. In no instance did this appear to inhibit the formation of callus. The functional end results in fractures of the elbow were curiously better than would be expected from the deformity and displacement in the x-ray picture and notoriously poor after prolonged immobilization or open operations intended solely to obtain anatomical position.

2. THE FOREARM

A. The Proximal Radius and Ulna.—Wires through the olecranon and distal radius were used in approximately 20 cases. In cases in which the olecranon was not available, the wire was inserted more distally in the ulna. Careful realignment of the proximal third of the radius was difficult to achieve. The ulna, however, could be controlled very well. An arrangement similar to that illustrated in Figure 1 was usually employed.

B. The Distal Radius and Ulna.—Traction through the metacarpals was used in approximately 10 cases of fractures of the distal radius and ulna. A nice adjustment of ulnar or radial deviation was necessary, and particular care was required to insert the wire and preserve the palmar curve of the hand. The wire did not always transect all four metacarpals, and the method was very difficult to apply even in the hands of an experienced technician. The patients were reluctant to exercise the fingers because of pain and because even the slightest fixation of the carpometacarpal joints interfered with the rotation, gliding, and interaction of the complicated, highly flexible joints of the hand.

C. The Radius.—Fractures of one of the forearm bones were less frequent than those of both bones. Fractures of the ulna alone did not require traction and could almost invariably be managed in plaster. Traction through the thumb metacarpal or the styloid process of the radius with the hand in ulnar deviation was a satisfactory method for fractures of the distal and middle thirds of the radius.

D. The Hand.—Traction was occasionally, but not often, necessary for fractures of the hand. No other group of fractures presented the problem of motion versus immobilization more acutely. Excellent anatomical realignment could often be obtained but at the expense of ankylosis. For many fractures, a middle course was achieved by the use of traction hooks inserted into the extensor surfaces of the middle phalanges. This method has been reported elsewhere and was used for fractures of proximal phalanges and multiple fractures of the metacarpal bones.[3]

3. Quigley, T. B., and Urist, M. R.: Interphalangeal Joints: Method of Digital Skeletal Traction Which Permits Active Motion, Am. J. Surg. **73**:175-183, 1947.

Fractures of the third and fourth metacarpals with an intact bone on each side were rarely significantly displaced and required only simple plaster splinting for three weeks at the most. At least as much time and effort were spent on these injuries as on fractures of the larger bones. In most hospitals, the surgery of the hand was assigned as the particular responsibility of one or two officers who would be able to accumulate enough experience to become proficient in the special problems of hand injuries. Ingenious devices were developed for active and resistance exercises during the period of rehabilitation. Early occupational and psychological treatment were also indispensable adjuncts to hand surgery.[1]

3. THE PELVIS

The highly accelerated vehicles and heavy machines of modern warfare produced displaced fractures of the pelvic ring of every description. These were nearly as numerous as the shattering compound wounds caused by missiles and have been

Fig. 2.—The so-called 90-90 traction suspension arrangement for extensive compound fracture of the hips and pelvis.

described in detail in a previous paper.[4] Injuries to every organ within the pelvic basin were seen, which, of course, demanded the highest priority in treatment. Once urinary and bowel function has been controlled and reestablished by cystotomy, urethotomy, and colostomy as required, treatment of bone injury became necessary. The position of the fractures could not be changed in many instances. Manipulations of every description were attempted in severe cases of deformity on an individual basis using such measures as acute flexion and rocking of the thighs on the abdomen, rotation of the pelvis through the trunk, traction through the lower extremities on the fracture table, and manipulation in lateral recumbency after the manner of Watson-Jones.[5] Once reduction had been effected, the elements of traction had to

4. Urist, M. R.: Management of Battle-Incurred Compound Fractures in the Region of the Hip Joint (Wellcome Award Essay, 1947), Mil. Surgeon **101**:467-489, 1947; Fracture-Dislocations of the Hip Joint: Nature of Traumatic Lesion, Treatment, Late Complications, and End Results, J. Bone & Joint Surg. **30**:699-727, 1948.

5. Watson-Jones, R.: Dislocations and Fracture Dislocations of the Pelvis, Brit. J. Surg. **25**:773, 1938.

be carefully analyzed and applied for immobilization of the fracture and nursing care of the patient. Lateral suspension of the pelvis by traction through the femoral condyles with the hips flexed at 90 degrees was often useful and surprisingly comfortable (Fig. 2). Certain extensive comminuted fractures with a tendency to collapse were maintained by lateral traction through both iliac crests and distal traction through the upper tibias or lower femurs. One such patient was comfortable for several weeks with sufficient traction distributed at these four points to suspend his weight. The Rouvillois or lumbofemoral suspension frame obtained from "liberated" medical depots in France was a more comfortable and effective apparatus from the nurses' point of view than the conventional hammock (Figs. 4*A* and *B*).

Fig. 3.—Roentgenogram showing a method of locating the approved sites of election for insertion of Kirschner wires in the lower femur and the tibial tubercle. The topographical anatomy is shown by means of barium sulfate paste applied to the skin. Iron washers have been laid on to show the place for insertion of the wires. This exercise was used as an adjunct to the method of palpation for teaching skeletal landmarks and orthopedic techniques to ward officers and general physicians.

4. THE FEMUR

Certain definite lessons were learned from experience with more than 1,000 fractures of the femur. In no other site of the body is the action of muscles more important in producing deformity, and in no other group of fractures was correct application of traction more important for the achievement of satisfactory alignment of the fracture.

The femoral condyles or the tibial tubercle was used as the site for the Kirschner wire, depending on the nature of the fracture and the position of the associated wounds (Fig. 3). A few important points may be suggested about the insertion of the wire through the lower end of the femur. It must be above the attachments of the collateral ligaments and posterior to the medial and lateral aspects of the

suprapatellar pouch. If the wire were inserted with the leg fully extended and the knee were later flexed in the splint, the skin and deep soft parts would become folded up or stretched around the wire, and ischemia and infection would be sure to follow. In no instance did damage to the knee joint occur as a result of traction through the tibia even though at times weight of the order of 30 lb. (13.6 kg.) was used for brief periods.

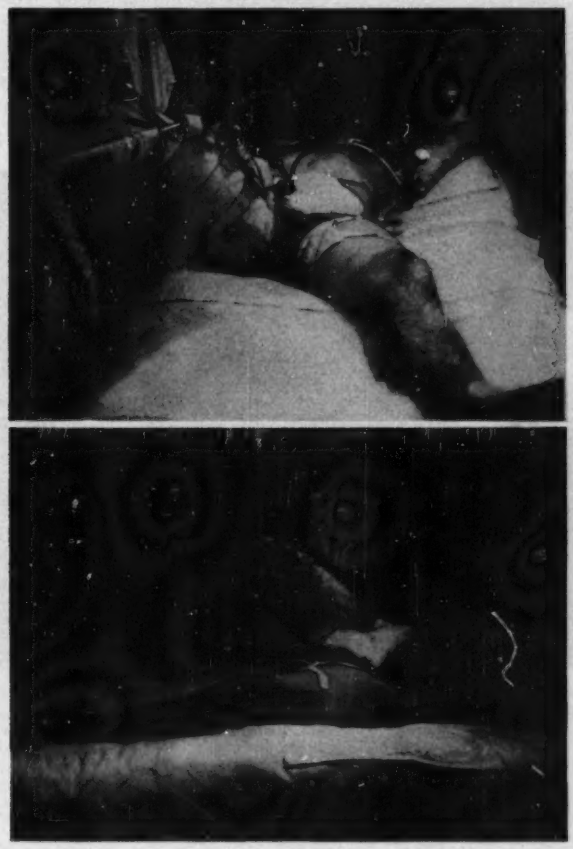

Fig. 4.—A compound comminuted fracture of the upper to middle third of the femur held in alignment in a Rovillois lumbofemoral splint. This was a comfortable apparatus for suspension and was commonly found in medical supply establishments in France.

A. The Neck and the Intertrochanteric Region.—In this group a coxa vara deformity was invariably present by the time the patient arrived from the field. Reduction was effected by manual traction and retained by continuous skeletal traction through the lower femur, with suspension in either an inverted Keller-Blake half-ring splint or the French lumbofemoral splint. It was found that if the half-ring

splint were used in the usual fashion, patients were uncomfortable, displacement was relatively uneffected and wound dressings were difficult.

B. The Upper Third of the Femoral Shaft.—This group of fractures was one of the few in which displacement followed a standard pattern. The proximal fragment was almost always flexed, abducted and externally rotated. Reduction by manipulation was usually successful, and the reduction could be maintained simply by lining up the distal fragment and the leg with the position of the upper fragment (Fig. 5).

C. The Shaft of the Femur.—Manipulation was necessary in approximately 40% of this group of fractures. Approximately 60% of the cases showed satisfactory position after suspension in skeletal traction and did not require manipulation. Fifty per cent contact of the fracture ends in two planes without overriding or angula-

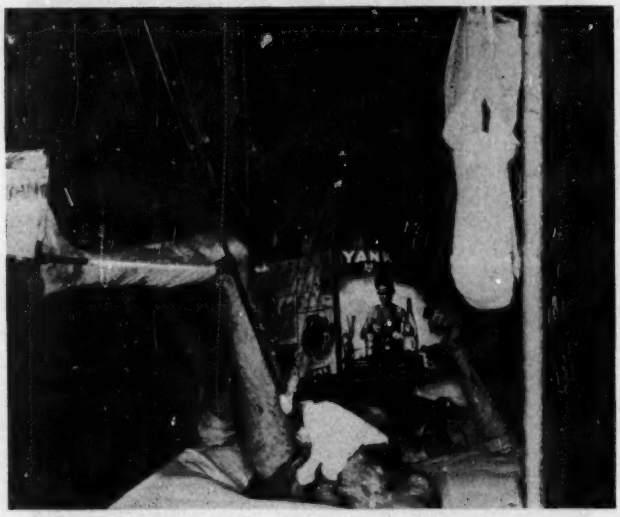

Fig. 5.—Skeletal traction for compound comminuted fracture of the upper third of the femur. The femur has been externally rotated, abducted, and flexed to correspond to the direction of muscle pull of the gluteus medius, iliopsoas, and short external rotator muscles of the hip which act on the short fragment of the upper femur. No other position of the limb was effective in holding a reduction of this type of fracture.

tion was the minimum acceptable position. Every effort was made to achieve at least 75% contact. Less than 50% contact of fracture faces was generally untenable. Displacement occurred insidiously, and roentgenograms taken four to six weeks after the institution of definitive traction would sometimes show unexpected loss of position and deformity leading to malunion or nonunion. Disability was greatly prolonged when massive callus had developed to overcome inadequate apposition or muscle interposition. Fortunately, the majority of fracture patterns were dentate, spiral, comminuted or "blown straw" in appearance and could be interdigitated well by manipulation. The question of muscle interposition arose often and was investigated at the time of secondary closure of the wound and in a few cases in which open

reduction was necessary. Only rarely was the interposed muscle in such mass and bulk as to form a barrier to normal healing. In almost all instances, the muscle was found to be attached to periosteum or callus at the fracture site and was in soft, hemorrhagic flaps which could be easily pushed aside by simple manipulation.

An interesting incidental observation on blood loss was made in several fractures of the femur which were submitted to incision and débridement of extensive wounds of the thigh prior to suspension in skeletal traction. At operation every effort was exerted to achieve and complete perfect hemostasis with the use of fine ligatures and endothermy. The amount of blood lost at operation was estimated by studies of the supernatant fluid after soaking all dressings, drapes, and gowns in a dilute solution of saponin. Two teams were in competition during these observations. The smallest amount of blood lost was 600 cc. The amount of blood lost on the field and during transportation was assumed to be equal to or more than this amount, and total blood replacement was nearly always desirable for fractures of the femur.

D. Supracondylar Fractures.—Shattering injuries of the lower third of the femur were the commonest of all war fractures of the femur. The distal fragment consisted of a fragment of any size varying from the entire lower third of the bone to one condyle only. The latter type is a fracture rarely seen in civilian practice from indirect violence. The main deforming factor is the pull of the gastrocnemius muscle. Lateral or forward displacement of the distal fragment was rare and easily corrected. The insertion of Kirschner wires in both the supracondylar region of the femur and the upper third of the tibia followed by manipulation by manual traction on the tautening bow at right angles was usually successful. The use of a posterior sling in place of skeletal traction from the distal fragment was unsatisfactory for healing of wounds and interfered with the circulation when applied to a swollen edematous thigh. In a few cases, simple suspension through the distal fragments with the hip and knee each flexed at 90 degrees was satisfactory. This position was also often used of necessity for the care of extensive soft tissue wounds of the posterior aspect of the thigh.

The "T-fracture" of the lower femur extending into the knee joint presented an interesting problem brought about by the differential pull of the two heads of the gastrocnemius muscle. After aspiration to relieve the severe pain in the knee joint when it is greatly distended with blood and bone marrow fat, the condyles could be palpated and manipulated more easily into a satisfactory position. Compression could be exerted manually, and a padded carpenter's clamp or mechanical device was rarely if ever necessary.

Fractures of the lower end of the femur with large open wounds of the knee joint were always a serious problem and were managed by a bold policy of arthrotomy, open manipulation followed by closure of the wound. Sepsis was surprisingly infrequent. Needless to say, large doses of penicillin were administered parenterally and implanted locally, although there is now great doubt as to the efficacy of the latter method.

5. THE TIBIA AND FIBULA

Traction wires were inserted in the os calcis for shattering wounds of the lower leg and in the lower tibia for those of the upper leg.

At first, the extremity was suspended in a Thomas splint with Pearson attachment. This method was found to have many disadvantages. A considerable struc-

ture of pulleys and ropes was necessary, which required daily readjustment and was at best likely to be uncomfortable. The Bohler-Braun method was also used in one form or another. This arrangement was found to have one important defect which outweighed its advantages. With the lower leg in traction on the Bohler-Braun cradle, the distal fragment was relatively immobile but the proximal fragment moved with the patient. A method which combines the best aspects of both methods of traction has been devised.[6] Briefly, this consisted of a plaster of Paris cylinder applied after reduction by manipulation. The cylinder extended from the groin to the heel with the knee flexed at about 45 degrees. Incorporated in the plaster were U-shaped loops of wire at the midthigh, the knee joint, and the malleoli. A Pearson attachment fitted with a pulley was fixed to the loops at the knee joint to obtain self-retained continuous traction on the leg in a cast. As much as 15 degrees of correction of angulation in both planes could be achieved in this apparatus by raising or lowering the end of the Pearson attachment or the position of the pulley. The plaster on the extensor or flexor surface of the leg was windowed as necessary for treatment and dressings of the wounds. The entire apparatus could easily be suspended with counterweights, and the patient could move in any direction without motion at the fracture site. Skin grafting was greatly facilitated, and it was even possible for patients in continuous traction to get about in wheelchairs. The apparatus was used at the 22d United States General Hospital for 65 compound fractures of both bones of the leg, including the ankle joint.

Fractures of the Foot.—Skeletal traction seemed advisable for approximately 15 cases of compound fractures of the midtarsal and metatarsal regions of the foot. Traction was applied by means of a vertical wire through the middle of the distal phalanx of the toes. The ends of wires were turned back to form hooks for elastics, which were attached to a metal hoop that was incorporated in a plaster cast. The combination of the plaster cast and the traction to hold the position of the fractures seemed effective but only after the fractures were reduced by a correctly applied manipulation and molded splint.

SUMMARY

The Kirschner wire, when used for continuous skeletal traction, should be inserted with the extremity and joints in the position in which they are later to be splinted or suspended. The incidence of skin necrosis and pin tract infection can be entirely eliminated by attention to this rule.

Skeletal traction without a preliminary manipulation of the fracture frequently fails to effect a satisfactory alignment of the bones. Experience has showed that the art of manipulation should be practiced and combined with properly applied traction in order to avoid unnecessary open operations and internal fixation for mass treatment of compound fractures received on the battlefield or during air attacks on civilian populations.

6. Urist, M. R.; Ries, L., and Quigley, T. B.: Plaster Traction Splint for Compound Comminuted Fractures of Tibia and Fibula, Surgery **23**:801-805, 1948.

EXPERIMENTAL OSTEOGENESIS IN RABBIT MUSCLE

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NEW BONE is created in the human body in (1) fetal osteogenesis and postfetal bone growth, the repair of fractures, cysts and inflammations, arthrodeses and bone-grafting procedures, and (2) in heterotopic bone formation. The latter is found most commonly in muscles, fascia and tendons but also in such varied tissues as severely damaged eyes, meninges of the brain, tonsils, lungs, thyroid gland, ovaries, uterine tube, pelvis, kidneys, scars of wounds and walls of arteries (Table 1). The development of bone in so great a variety of tissues indicates a potential universality in its growth, especially within tissues of mesenchymal origin. Although there are many similarities between normal osteogenesis

TABLE 1.—*Types of Bone Formation*

I. Growth and Regeneration	II. Heterotopic Bone Formation
A. Fetal osteogenesis	A. Muscles (myositis ossificans)
B. Postfetal bone growth	B. Tendons and fascia
C. Repair of fractures	C. Lungs (e. g., tuberculosis, silicosis)
D. Arthrodesis	D. Scars of wounds
E. Bone grafts	E. Walls of arteries
F. Inflammations	F. Meninges of brain, damaged eyes, kidneys

and the heterotopic form, there is no sufficient evidence that these processes are identical. The first group represents manifestations of growth and regeneration in normal phylogenetic sites as contrasted with the second group of heterotopic bone formation which is extraskeletal. The common etiologic factor in the latter appears to be an irritating stimulus (degeneration or inflammation) which evokes a reparative response in fibroblastic tissue, which then differentiates into bone.

PREVIOUS WORK

In recent years there have been reports of attempts to extract from tissues a chemical substance which will induce heterotopic bone formation in extraosseous tissues. The literature has been previously reviewed by us and by others.[1]

From the Orthopedic Service, Mount Sinai Hospital, R. K. Lippmann, M.D., Director.

1. (*a*) Annersten, S.: Experimentelle Untersuchungen über die Osteogenese und die Biochemie des Fracturcallus, Acta. chir. Scandinav. (Supp. 60) **84**:1, 1940. (*b*) Bertelsen, A.: Experimental Investigations into Post-Foetal Osteogenesis, Acta. orthop. Scandinav. **15**:139, 1944. (*c*) Hartley, J. H.; Tanz, S. T., and Schneider, M.: Osteogenesis Produced by a Chemical Extract of Bone, J. Mt. Sinai Hosp. **15**:383, 1949. (*d*) Heinen, J. H., Jr.; Dabbs, G. H., and Mason, H. A.: Experimental Production of Ectopic Cartilage and Bone in the Muscles of Rabbits, J. Bone & Joint Surg. **31-A**:765, 1949. (*e*) Levander, G.: Study of Bone Regeneration, Surg., Gynec. & Obst. **67**:705, 1938.

Levander [2] was the first to inject alcoholic extracts of homologous young rabbit bone into the thigh muscles of mature rabbits. He obtained new bone formation in 22% of 70 animals. None of 80 controls, 60 with alcohol alone and 20 with alcoholic extracts of other tissues showed bone formation. Annersten [1a] injected concentrated homologous alcoholic extracts and obtained bone or cartilage formation in half of the rabbits, whereas when he injected heterologous extracts of calf bones only one-fourth of these animals showed a positive reaction. Bertelsen [1b] found acid-alcohol extracts of homologous bone marrow to yield the best results, with 10 of 12 positive reactions (83%). Annersten and Bertelsen both encountered isolated positive results in various controls. Bertelsen reported positive reactions in the following control experiments: one of 13 in which tendon extracts were used; two of 33 in which alcoholic injections with calcium and phosphorus added were used; one of 10 in which kidney extracts were used, and one of six in which acid alcohol was added to dialyzed urine. Rendano [3] felt that there was nothing specific in the reactions that could not be explained by the effect of alcohol alone. He obtained cartilage in one of 22 rabbits given injections of alcoholic extracts of bone, whereas six controls had negative reactions. Martin Lagos and Zarapico Romero,[4] after injecting 40% alcohol, found new bone in seven of 87 instances (8%). Heinen, Dabbs and Mason,[1d] after repeated injections of 3 cc. of 40% alcohol, found cartilage or bone or both in 23 of 37 triceps (62%), and 12 of 40 quadriceps (30%). Since some of their positive results were obtained after injections of calcium chloride (an irritant contained in alginate gel), they contested the claim of Blum [5] that calcium, phosphorus and phosphatase solution mixed with alginate gel implanted in skeletal muscle leads to the formation of heterotopic bone as a result of the solution. Slessor and Wyburn [6] repeated Blum's experiments and were unable to confirm his results. They pointed out that, in vitro, the alginate gel did not take up the solution but formed a soft ball of jelly in the center of the solution. Severi [7] referred to two patients reported in the literature by others in whom bone had formed at the site of quinine injections into muscle for the treatment of malaria. This stimulated him to experiment with repeated injections of quinine chloride (from two to ten times in each rabbit muscle). In five of 15 cases cartilage or bone was formed.

This review of research to date indicates that induced heterotopic cartilage or bone or both will form in skeletal muscle of rabbits in response to the injection of various irritants.

METHODS

We performed an initial experiment reported previously [1c] in which 95% alcoholic extracts were prepared from the ends of long bones of growing rabbits composed of growing epiphyses, cortex, and marrow. Three injections of 3 cc. of the extract at 48-hour intervals into the rectus

2. Levander, G., and Willstaedt, H.: Alcohol-Soluble Osteogenetic Substance from Bone Marrow, Nature, London **157**:587, 1946, Levander.[1e]

3. Rendano, C.: Su di un particulare principio osteogenetico contenuto nelle ossa normali, Ann. ital. di chir. **21**:249, 1942.

4. Martin Lagos, F., and Zarapico Romero, M.: Obtención experimental de hueso metaplasico, Trab., Inst. Nac. Cien. Med. **6**:173, 1946.

5. Blum, G.: Phosphatase and Repair of Fractures, Lancet **2**:75, 1944.

6. Slessor, A., and Wyburn, G. M.: Phosphatase and Bone Formation, Lancet **1**:212, 1948.

7. Severi, R.: Produzione sperimentale di cartilagne e di osso in sequito ad iniezioni di un sale di chinino, Pathologica **25**:611, 1933.

femoris muscles of young rabbits resulted in new borne formation locally in three of 11 animals. In none of 11 controls in which 95% alcohol alone was used on the opposite thigh of the same animal did cartilage or bone form. In our present experiments fresh rabbit marrow was separated from the bony cortex and separate 50% alcohol extracts of the marrow and cortex were made. Lipid, phospholipid, and fatty acid fractions of bone and bone marrow were also tested.

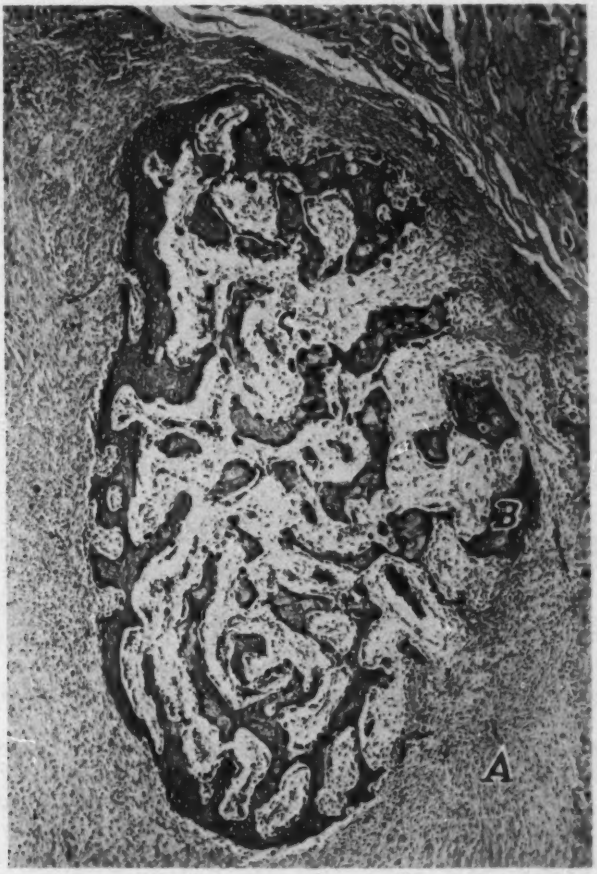

Fig. 1.—Bone formation in center of rabbit skeletal muscle (*A*), with newly formed trabeculae (*B*) and marrow (*C*), 28 days after a single injection of 1 cc. of a 50% alcoholic extract of fresh rabbit marrow. Paraffin section stained with hematoxylin and eosin (× 150).

Similar extracts were made of calf marrow and bone. Two additional series of control experiments were performed, using 1 cc. of 50% alcohol alone and 0.5 cc. of 5% quinine-urea hydrochloride. In the earlier experiments multiple injections of 3 cc. of 95% alcohol or alcoholic extracts caused widespread necrosis and secondary inflammation. The technique of employing single injections of small volume was adopted. The use of the triceps as an injection site was discontinued because of its relatively small size in relation to the volume of fluid injected. The

fluid was injected carefully into the center of the muscle mass of the rectus femoris, with the needle at about an angle of 45 degrees, special care being taken to avoid any contact with bone and to keep it away from the musculotendinous junction.

FINDINGS

The morphological findings were identical with those reported by previous workers in this field.[8] Grossly, the injection sites were indurated and cut with resistance or a gritty sensation. Microscopically, there was evidence of degeneration and necrosis of skeletal muscle fibers with a young connective tissue response of repair. In some regions the stellate cells of mesenchymal tissue showed increase of the mass of protoplasm about the nuclei (endoplasm), and in other regions this type of transformation was further advanced, with the endoplasm becoming granular, more confluent and homogenous (exoplasm). This presented a precartilaginous appearance in some areas. When the reaction had differentiated further it took on a hyaline appearance, with definite cartilage formation or formed bone.

TABLE 2.—*Results of Experiments*

Substance Injected	Total No. of Experiments	Total No. of Positive Reactions*	Duration in Days
Alcoholic extract of ends of long bones of very young rabbits †....	11	3	53
Alcoholic extract of fresh rabbit marrow ‡.....	16	5	28
Alcoholic extract of fresh rabbit long bone cortex (no marrow) ‡..	36	0	29
Aqueous extract of fresh rabbit long bones, cortex and marrow....	8	0	18-24
Alcoholic extract of residue of the above aqueous solution ‡.....	8	3	18-24
Lipoid fraction of fresh young rabbit marrow.....	34	3	27-31
Phospholipid fraction of young rabbit marrow.....	4	0	23
Fatty acid fraction of young rabbit marrow.....	7	1	18-30

* Chondrogenesis or osteogenesis or both appearing inside the muscle mass at the site of injection.
† This experiment was reported previously.[1c] Three injections of 3 cc. at 48 hour intervals.
‡ 50% alcoholic solution.

In some specimens cartilage alone was present, in others cartilage and bone, and in others only bone.

Bone appeared either by direct transformation from the connective tissue or by enchondral ossification. A reaction was not reported as positive unless cartilage or bone was present microscopically.

Of 16 experiments using concentrated alcoholic extract of fresh rabbit marrow employing one injection of 1 cc., five showed the development of new bone or cartilage or both (Fig. 1). Concentrated alcoholic extract of fresh rabbit long bone cortex with all the marrow completely removed did not produce any cartilage or bone in 36 experiments (Table 2). This group of rabbits was larger and older than that used in previous experiments. Aqueous extracts of fresh rabbit long bones including both cortex and marrow produced negative results in eight instances whereas alcoholic extracts of the residue produced three positive results out of eight experiments. This experiment suggested that the postulated osteogenetic stimulating factor was not water soluble, but remained in the residue, and was then extracted with alcohol. These results were about the same as those found with alcoholic extract of marrow, implying that the potency was not impaired by

8. Annersten.[1a] Bertelsen.[1b] Heinen and others.[1d] Levander.[1e]

the aqueous extraction. On the other hand, perhaps the aqueous solution failed to produce bone, since it lacked the irritating quality of the 50% alcohol solution. Lipid, phospholipid, and fatty acid fractions from an alcoholic solution of fresh rabbit marrow resulted in fewer positive results. In 34 experiments with the lipid extract there were only three positive reactions. In four experiments with the

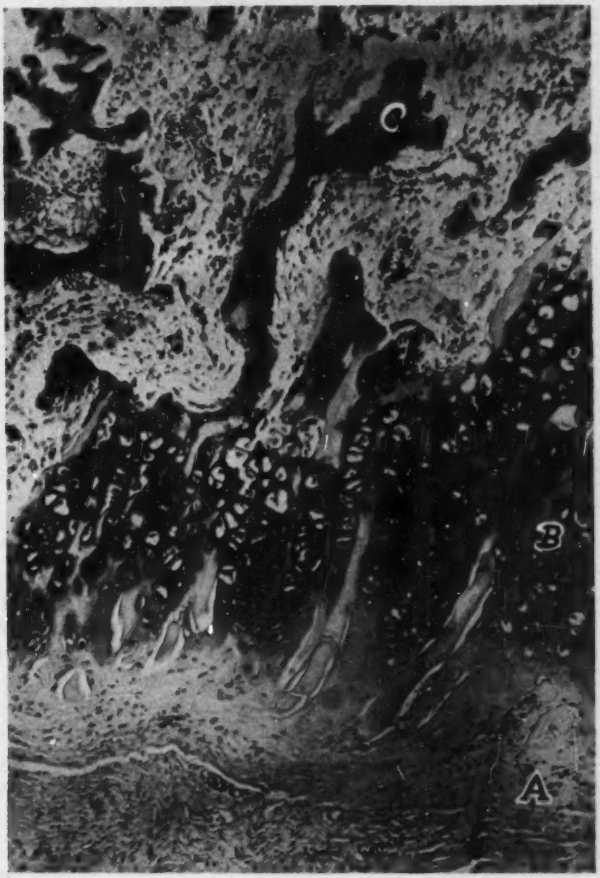

Fig. 2.—Bone formation in center of rabbit skeletal muscle (*A*), with irregular columns of cartilage (*B*) forming bony trabeculae (*C*), by enchondral ossification, 28 days after a single injection of 1 cc. of 50% alcohol. Paraffin section stained with hematoxylin and eosin (× 200).

phospholipid fraction there were no positive results, and in seven experiments with the fatty acid fraction there was one positive result. The lipid, phospholipid and fatty acid fractions were first dried and redissolved in alcohol. As is so common in dealing with biological products, drying may have either weakened or destroyed

any possible osteogenetic substance contained therein. With the use of only 1 cc. of 50% alcohol there were two positive results in 27 additional controls (Fig. 2). This result was in accordance with the findings of other workers that alcohol alone can produce cartilage or bone or both.[9] Single 0.5 cc. injections of 5% quinine-urea were given into the thigh muscles of rabbits. No cartilage or bone formed in 34 experiments.

The authors repeated part of Annersten's work using heterologous extracts. Fresh and refrigerated calf and beef marrow and bone were used. Fewer positive reactions were obtained with extracts of this material (Table 3). Fifty per cent alcoholic extracts of fresh calf marrow obtained from a slaughter house yielded five positive reactions out of 32 experiments, and alcoholic extracts of refrigerated calf and beef marrow furnished three positive reactions out of 21 experiments. Fatty acid fractions of the fresh calf marrow resulted in one positive reaction in eight experiments, as did the phospholipid fraction. Interestingly enough, these last

TABLE 3.—*Results of Injection of Heterologous Extracts*

Substance Injected	Total No. of Experiments	Total No. of Positive Reactions*	Duration in Days
Controls			
50% alcohol 1 cc.	27	2	24-28
Urea and quinine 5% 0.5 cc.	34	0	29
Calf marrow and bone			
Alcoholic solution of fresh calf marrow †	32	5	27-31
Alcoholic extracts of refrigerated calf and beef marrow from hospital butcher's refrigerator †	21	3	18-42
Fatty acid fraction of fresh calf marrow †	8	1	20-35
Phospholipid fraction of fresh calf marrow †	8	1	20-35
Fatty acid fraction refrigerated calf and beef marrow †	2	0	23

* Chondrogenesis or osteogenesis or both appearing inside the muscle mass at the site of injection.
† 50% alcoholic solution.

two positive reactions occurred in the same animal, one in the right thigh and the other in the left thigh. The findings in this young rabbit raised the interesting question of whether or not certain experimental animals have a propensity for heterotopic bone formation. Heinen and others concluded that younger animals (one month old) formed larger amounts of more mature cartilage and bone than older rabbits after the injection of alcohol alone or calcium chloride. Factors besides age might influence some rabbits to form heterotopic bone much more easily than others. Fatty acid and phospholipid extracts of refrigerated beef bone (taken from a butcher's refrigerator) yielded no positive results.

COMMENT

That a specific osteogenetic stimulating substance exists in nature can be inferred from observations of osteogenesis during growth, the healing of a fracture or the effect of a bone graft. In bone growth some factor intrinsic to the growing organism produces osteogenesis. In the healing of a fracture, external trauma possibly liberates chemical factors which stimulate new bone formation. In the application of a bone graft, some additional osteogenetic stimulus seems to be added to the local

9. Heinen and others.[1d] Martin Lagos and Zarapico Romero.[4]

site which causes bony union in a great many instances. Specific inductors of osteogenesis probably exist, but how they operate is still obscure. The search for an osteogenetic substance, however, seems logical. Whether experimentally induced heterotopic bone formation in the skeletal muscles of rabbits has any relation to osteogenesis of growth and regeneration is not known. That induced heterotopic bone formation is a nonspecific reaction is indicated by the variety of irritants that produce a mesenchymal reaction of repair which differentiates into cartilage or bone or both. In some instances this will result after a single injection, whereas in others multiple injections seem necessary. It is not certain that alcohol is the best solvent for the postulated osteogenetic substance. The reports of Annersten and Bertelsen suggest strongly that lipid solvents give the best results, but it remains to be conclusively demonstrated that the reactions are not the result of their irritating qualities. Rabbits may not be the most suitable animals for this type of experimentation. Younger rabbits and probably certain species tend to form bone more easily.

CONCLUSIONS

1. Heterotopic bone and/or cartilage can be produced in rabbit skeletal muscle (rectus femoris) at the site of injection of various substances.

2. Although various extracts (50% alcohol, lipid, phospholipid, fatty acid) of bone and bone marrow of rabbits and calves produced bone and/or cartilage at the site of injection into rabbit skeletal muscle, the reaction is probably nonspecific and may be the result of the irritating qualities of the material injected or its solvent.

Paul Klemperer, M.D., Sadao Otani, M.D., and Harry Sobotka, Ph.D., gave advice during the course of this investigation. Miss Sarah Spector gave technical assistance.

PILONIDAL CYSTS AND SINUSES

A Statistical Review

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AND
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THE MERITS of the various surgical procedures for the treatment of pilonidal cyst and sinuses are difficult to evaluate from the many reports in the literature. This evaluation is incomplete in many series because of lack of information in reference to the follow-up period and to the percentage of the total number of cases actually followed. A compilation of the reports found in the literature has been tabulated according to the method of surgical treatment. In this manner an over-all picture may be obtained in a comparative way of the end results in each group. In addition the results of a survey of our cases will be given.

REVIEW OF RESULTS IN THE LITERATURE

A survey conducted and reported by Kleckner [1] in 1936 of the surgical methods preferred by members of the American Proctologic Society for the treatment of this condition revealed that 87% of the surgeons preferred the open method and only 7.5% advocated primary closure, whereas 5.5% used both methods or were undecided as to the method of choice.

In many instances, the decision for an open or closed method was based on the presence or absence of infection. In several reports excision and primary closure were performed in cases showing no infection or mild chronic infection.[2] In cases with evidence of gross infection and drainage, the open method was used.[3] Some surgeons feel that if acute infection is treated by incision and drainage and hot wet packs primary closure is still permissible.[4] On the other hand, Kleckner has emphasized that treatment of a sinus once infected requires open methods.[1]

From the Department of Surgery, Veterans Hospital, Des Moines, Iowa. Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Kleckner, M. S.: Pilonidal Sinus, Tr. Am. Proct. Soc. **37**:166, 1936.

2. (*a*) Hamilton, H. H.; Custer, B. S., and Kellner, A.: Pilonidal Cyst: An Analysis of 132 Consecutive Cases, New England J. Med. **231**:757, 1944. (*b*) Kooistra, H. P.: Pilonidal Sinuses, Am. J. Surg. **55**:3, 1942.

3. (*a*) McKirdie, M.: Pilonidal Sinus, Ann. Surg. **107**:389, 1938. (*b*) Parker, M. L.; Menaker, G. J., and Miller, D. M.: Surgical Principles in the Treatment of Pilonidal Cysts and Sinuses, J. Internat. Coll. Surgeons **12**:30, 1949.

4. (*a*) Ferguson, L. K., and Mecray, P. M., Jr.: Pilonidal Cysts: Excision and Primary Suture in Ambulatory Patients, Am. J. Surg. **36**:270, 1937. (*b*) Swinton, N. W., and Jackson, D., Jr.: Pilonidal Cysts and Sinuses, S. Clin. North America **29**:879, 1949.

Dunphy, who stated that primary closure is suitable for 60% of cases, has listed definite indications for the open-pack method: (*a*) large sinuses and fistulous tracts, (*b*) recent acute infections, (*c*) marked obesity, and (*d*) gross contamination in attempted primary closure.[6]

Holman has noted that the presence of dead space provides the greatest obstacle to healing after primary closure. Added factors inherent in the area of the wound include excessive moisture, heat, motion, and trauma.[6] Recurrence of symptoms or failure to heal after primary closure may be due to inadequate excision of the sinus tract,[7] but also responsible is unobliterated dead space and residual infection.[8]

Several surgeons think that primary closure should be attempted except in severe infection, since even if the wound breaks down it will then heal by granulation and nothing is lost.[9] This method may, however, result in loss of time to

TABLE 1.—*Open Method—Excision and Packing*

Author	Number of Cases	Number of Cases Followed	Follow-Up Time	Percentage of Failure or Recurrence
1. Breidenbach and Wilson *	122	32	2-14 mo.	6
2. Burns †	106	65	.....	23
3. Dunphy and Matson [5]	23	..	.....	4.3
4. Kleckner (survey of proctologists) ‡	4,231	..	.....	1.13
5. Kleckner §	160	160	1 yr. or more	0
6. Koolstra [8b]	24	24	.....	21
7. MacFee ‡	36	32	6 mo. or more	16.7
8. McKirdie [8a]	11	11	.....	63
9. Rogers and Hall §	75	..	.....	21.5
10. Silverman ‖	14	14	.....	21.4
11. Swinton and Jackson [8b]	54	30	.....	3.3
12. Theis and Rusher ¶	29	..	.....	3.5
Total	4,895	389	.....	17
Excluding Series Number 8	4,884	..	.....	12.7

* Ann. Surg. **102**: 455, 1935.
† Arch. Surg. **52**: 33 (Jan.) 1946.
‡ Ann. Surg. **116**: 687, 1942.
§ Arch. Surg. **31**: 742 (Nov.) 1935.
‖ New York J. Med. **39**: 1598, 1939.
¶ Surg., Gynec. & Obst. **79**: 482, 1944.

the patient since a longer period of observation in the hospital is usually necessary after primary closure than after the open method.

The total number of cases reviewed in which treatment was by the open method (including Kleckner's survey of 4,231 cases gathered from many of the country's proctologists) was 4,895 (Table 1). The percentage of failure or recurrence ranged from 0% in Kleckner's personal series of 160 cases to 63% in 11 cases reported by McKirdie.[8a] Excluding the latter report, the average rate of recurrence was 12.7% in 4,884 cases of treatment by the open method.

5. Dunphy, J. E., and Matson, D. D.: The Treatment of Pilonidal Sinus, Surg., Gynec. & Obst. **75**:737, 1942.

6. Holman, E.: Pilonidal Sinus: Treatment by Primary Closure, Surg., Gynec. & Obst. **83**:94, 1946.

7. Larkin, L. C.: Pilonidal Cyst, Surg., Gynec. & Obst. **82**:694, 1946.

8. (*a*) Cantor, A. J.: Pilonidal Dimple, Sinus, Cyst and Abscess, J. Internat. Coll. Surgeons **8**:514, 1945. (*b*) Larkin.[7]

9. Cantor.[8a] Parker and others.[8b]

Primary closure was used in 1,184 reported cases, with a recurrence rate ranging from 2% in 43 of Hamilton's cases to 53% in 19 other cases reported by Hamilton [2a] (Table 2). In the first group of patients, no infection was present, while a moderate infection was present in the group of 19 patients. Excluding the latter group, the average rate of recurrence was 21.9% of 1,165 reported cases in which the primary closure method was used for treatment of pilonidal cysts.

Three hundred and seventy-seven patients were treated by means of partial closure, which resulted in a rate of recurrence of from 6.6% in 76 cases reported

TABLE 2.—*Primary Closure Method*

Author	Number of Cases	Number of Cases Followed	Follow-Up Time	Percentage of Failure or Recurrence
1. Breidenbach and Wilson *	29	18	2-14 mo.	44
With drainage	27	7	.....	24
2. Burns †	65	43	.....	30
With drainage	36	22	.....	41
3. Dunphy and Matson [5]	33	..	.....	6
4. Ferguson and Meeray [4a]	38	37	26 cases 1-4 yr.	8
5. Hamilton and others [2a]				
a. No infection	43	..	.....	2
b. Mild infection	20	..	.....	10
c. Acute and chronic infection	19	..	.....	53
6. Kleckner (survey of proctologists) [1]	365	..	.....	23.29
7. Koolstra [2b]	24	24	.....	21
With drainage	29	29	.....	34
8. Larkin [7]	100 (13 partial)	100	14 mo.	5
9. MacFee ‡	34	33	6 mo. or more	32.3
10. McKirdie [3a]	68	45	.....	31
With drainage	..	..	.....	..
11. Mohardt §	92	51	.....	15
12. Rogers and Hall ‖	41	41	.....	37
13. Russel ¶	20	20	18 mo.	10
14. Silverman ‡	10	10	.....	30
15. Swinton and Jackson [4b]	46	21	.....	10
16. Theis and Rusher **	45	..	.....	15.5
Total	1,184	..	.....	23.4
Excluding Series 5c	1,165	..	.....	21.9

* Ann. Surg. **102**: 455, 1935.
† Arch. Surg. **52**: 33 (Jan.) 1946.
‡ Ann. Surg. **116**: 687, 1942.
§ Surg., Gynec. & Obst. **89**: 425, 1949.
‖ Arch. Surg. **31**: 742 (Nov.) 1935.
¶ Canad. M. A. J. **60**: 267, 1949.
‡ New York J. Med. **39**: 1598, 1939.
** Surg., Gynec. & Obst. **79**: 482, 1944.

by Theis and Rusher to 75% in 25 cases reported by Rogers and Hall (Table 3). Again excluding the series with an exceptionally high rate of recurrence, failure of cure resulted in 18.5% of 352 patients with pilonidal cysts treated by partial closure.

CLINICAL MATERIAL AND RESULTS

To evaluate the results of pilonidal cyst surgery at this hospital, follow-up investigation was attempted on the patients operated on during the three-year period from Sept. 1, 1946, to Sept. 1, 1949. One hundred and seventy-two surgical procedures were performed (excluding incision and drainage) on 171 patients. The open method of excision and packing was used in 151 cases; excision and primary closure was the operation carried out in 5 cases, and 16 patients were

treated by marsupialization. The surgery was performed by 21 different surgeons. Spinal anesthesia was given exclusively. The diagnosis was confirmed in all instances by pathologic examination.

Postoperative treatment in the open method cases consisted of simple cleanliness with the use of sitz baths, packing with dry dressings and mechanical prevention of "bridging." Antibiotics were administered in most cases.

TABLE 3.—*Partial Closure Method**

Author	Number of Cases	Number of Cases Followed	Follow-Up Time	Percentage of Failure or Recurrence
1. Breidenbach and Wilson *	79	24	2-14 mo.	37
2. Burns †	6	6	.....	17
3. Dunphy and Matson §	5	..	.....	20
4. Koolstra ¶	10	10	.....	20
5. MacFee ‡	147	116	6 mo. or more	12.9
6. McKirdie **	6	5	.....	20
7. Rogers and Hall §	25	..	.....	75
8. Silverman ‖	22	23	.....	26
9. Theis and Busher ¶	76	..	.....	6.6
Total	377	..	.....	24.1
Excluding Series 7	352	..	.....	18.5

* See footnotes to table 1.

TABLE 4.—*Type of Surgery Performed*

	No. of Cases	No. of Cases Followed			No. of Patients Cured	Percentage Cured
		Letter	Personal	Total		
Open	151	76	37	113	107	94.7
Primary closure	5	2	2	4	3	75
Marsupialization	16	13	2	15	15	100
Total	172	91	41	132	125	89.9 (Average)

TABLE 5.—*Previous Surgery in Patients Followed*

Present Surgery	Incision and Drainage	Open Method	Primary Closure	Type Not Known	No. of Patients Cured	Percentage Cured
Open	36	2	9	1	47	98
Primary closure	1	..	..	..	1	100
Marsupialization	3	..	..	..	3	100

A questionnaire type of letter was mailed to all patients. Forty-one patients came to the hospital for personal evaluation, while 91 returned the questionnaire with the information requested, a total of 132 patients followed up, or 76.7%. The follow-up time ranged from nine to 44 months. The patients were classified as cured of their pilonidal cyst if no further medical or surgical treatment was administered and the wound was solidly healed. On this basis, of 113 patients followed who were treated by the open method, 107, or 94.7%, were cured. Primary closure or marsupialization of the cyst was carried out in an insufficient number of patients to be statistically significant; however, of five patients on whom primary

closure was done, four were followed, with three cured (75%). Marsupialization was carried out on 16 patients, with follow-up on 15 patients, all of whom were cured (Table 4).

Fifty-two patients had been subjected to some type of surgical procedure previous to their admission to this hospital. Of the 36 patients who previously underwent incision and drainage, several had undergone the procedure more than once. In four patients the acutely inflamed cysts were incised and drained during their hospitalization before definitive surgery was accomplished. All of these 52 patients were treated by the open method, and over 98% were cured (Table 5).

TABLE 6.—*Infection on Admission of Patients Followed*

	Acute			Chronic			None		
Present Surgery	No. of Cases	No. Cured	Per Cent Cured	No. of Cases	No. Cured	Per Cent Cured	No. of Cases	No. Cured	Per Cent Cured
Open	6	6	100	87	82	94.2	7	6	85.4
Primary closure	..	..	...	2	2	100	2	1	50
Marsupialization	1	1	100	10	10	100	2	2	100

TABLE 7.—*Symptoms and Complaints Following Surgery*

	Number of Cases	Drainage	Mild Pain in Area of Scar	Fissure in Scar	Total
Open	113	3	15	3	21
Primary closure	4	1	1	..	2
Marsupialization	15	2	1	..	3

TABLE 8.—*Postoperative Complications During Hospitalization*

Slight separation of wound following primary closure	3
Bleeding of wound following open method	7

TABLE 9.—*Average Hospital Stay (in Days)*

Open method of treatment	17.2
Primary closure	22.4
Marsupialization	16.9

Six patients presented acutely infected cysts on their admission. Three cysts were incised and drained previous to excision and open packing, and three were initially treated by the open method. Marsupialization was used in one additional case. All of the seven patients were cured. Antibiotics were almost always given in the acutely infected cases (Table 6).

In the follow-up of the 113 patients treated by the open method, postoperative symptoms consisted of drainage in three patients (two patients having results classified as failures). Another patient in whom the result was classified as a failure did not mention his recurrent symptoms. Fifteen patients remarked that they occasionally experienced mild soreness over their scars. Three other patients who were personally examined presented a very small superficial fissure in the natal cleft, unnoticed by them, which was associated with excessive perspiration

and lack of cleanliness. Four patients were followed who were treated by primary closure, and one of these, with a result classified as a failure, reported drainage as a recurrent symptom. This patient was subsequently cured by the open method. Two of the 15 patients in whom the cyst was marsupialized reported transient drainage which subsided without further medical treatment (Table 7).

Postoperative complications which occurred while the patient was in the hospital consisted of slight separation of the wound in three of the five patients treated by primary closure and postoperative hemorrhage of mild degree in seven of the 151 patients who were handled by the open method. Control by suture was necessary in only one instance (Table 8).

The total hospital stay was 17.2 days for patients treated by the open method, 22.4 days for patients in whom primary closure was used, and 16.9 days for patients treated by marsupialization (Table 9).

SUMMARY AND CONCLUSIONS

One hundred and seventy-one patients have been treated surgically for pilonidal cysts during a three-year period from 1946 to 1949, with a follow-up period ranging from nine to 44 months. Of this number, 151 patients were treated by the open method of incision and packing of the wound, 16 by marsupialization, and 5 by excision and primary closure. Seventy-seven per cent of the total number of patients were followed by means of a letter or personal examination. The open method of treatment resulted in a cure rate of 94.7%; an insufficient number of patients were treated by other methods to be statistically significant.

A review of the results reported in the literature together with an evaluation of our own series of cases demonstrates that the open method of excision and packing results in the greatest number of cures for the treatment of pilonidal cysts and sinus disease.

MODIFIED HOKE TRACTION APPARATUS

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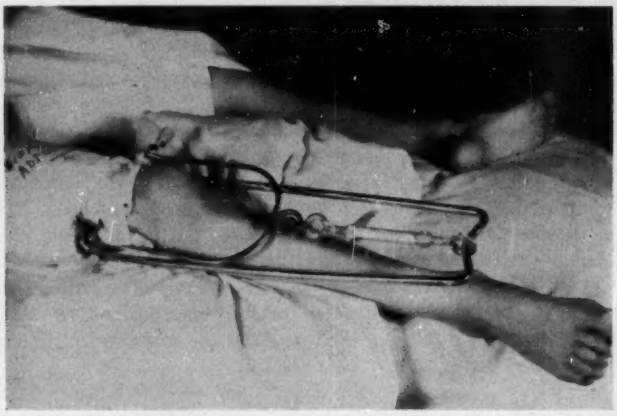
A VERY efficient type of traction, originally used by Hoke and known as the "Hoke-Martin Plaster Traction," [1] is often overlooked when strong fixed traction is desired. As originally described, a plaster hip spica is applied extending from the nipple line down to and incorporating the foot on the well side and down to just above the knee or to the lower part of the leg on the affected side. Two metal bars, joined at the end and between which a ratchet is placed 2 in. (5 cm.) from the end, are incorporated into the plaster on the affected side. Either skeletal traction or skin traction can be applied to the extremity, above or below the knee as required.



Modified Hoke traction using a turnbuckle.

Herein is described a modification of the apparatus which is very useful in conditions such as old or "irreducible" congenital dislocation of the hip, old fracture dislocations, when it is desired to bring the femoral shaft down in relation to the pelvis prior to surgery, and, possibly, in fresh fracture dislocations or simple dislocations of the hip when strong traction is required.

The hip spica is applied in the usual manner but extending to above the knee only on the affected side. A Pearson attachment is then incorporated in the plaster on the affected side, but first the stays are removed from the tips of the bars of the frame, and a large turnbuckle is threaded over the bars and anchored at the end. The Pearson attachment extends well beyond the knee. A Steinmann pin or Kirschner wire is then driven across the distal femur and a traction stirrup applied and then fixed to the turnbuckle. By manipulation of the turnbuckle, strong traction can be applied effectually to the femur on the affected side.

3½ E. Gordon St.

From the Department of Orthopaedics, University of Virginia Hospital.

1. Hoke, M.: The "Hoke Martin Plaster Traction" Apparatus, in Campbell's Operative Orthopedics, edited by J. S. Speed, St. Louis, C. V. Mosby Company, 1949, Vol. 1, p. 48.

Case Reports

RECURRENT ABDOMINAL PAINS DUE TO LIPOMA OF ILEUM

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AND
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DOTHAN, ALA.

LIPOMA of the ileum is a rare disease and usually manifests itself by recurring attacks of abdominal pain finally resulting in acute intussusception. In 50,775 surgical specimens examined by Merchant,[1] only six benign tumors of the small bowel were found. In reviewing 7,340 autopsies, he found only 18 cases of benign tumors of the small bowel. Raiford[2] found 88 cases of a similar lesion in 11,500 autopsies and 45,000 surgical specimens. Merchant concluded that the incidence of benign tumors of the small intestine was 8.7% of all neoplasms in the intestinal tract. Shottenfeld[3] was able to collect 275 cases of gastrointestinal lipomas from the world literature. Fifty-six per cent of these occurred in the small intestine, and 52% of those occurring in the small intestine occurred in the ileum.

As indicated from the statistics given above, a larger percentage of benign tumors of the small bowel are found at autopsy than in surgical specimens. This probably results from a lack of symptoms produced by these tumors. The condition which results in surgical exploration is usually intestinal obstruction, which is in most cases due to intussusception. Twenty-three per cent of small bowel tumors in Raiford's series and 44% in Shottenfeld's collected series of cases produced intussusception.

The following case well illustrates the type in which multiple bouts of previous intestinal obstruction have occurred with intervals of complete freedom of symptoms between attacks. It also illustrates the typical pathological process found in ileal lipoma associated with intussusception and acute intestinal obstruction.

A 71-year-old Negro woman entered the hospital on July 14, 1950, complaining of generalized cramping abdominal pain and pain in the right lower quadrant. Her present illness began three days before her admission to the hospital, when in the early morning she began having severe cramping pains in the lower abdomen and in the periumbilical area. This was followed by nausea but no vomiting. The pain increased in severity until it was of a "doubling up" character and persistent. The nausea partially subsided. She was never completely free of pain. She had no blood in her stools, and her bowel habits were regular and normal.

Her past history revealed frequent bouts of severe cramping abdominal pain. These started in late adolescence, were recurrent, and had on numerous occasions been associated with nausea and vomiting; on each of the previous occasions the attack would clear up completely, leaving her without residual complaint. She never had melena or hematemesis. She had otherwise been in normal health except for premenopausal dysmenorrhea.

1. Merchant, F. T.: Intussusception Due to Hemangioma of the Jejunum, Arch. Surg. **39**:1031-1040 (Dec.) 1939.

2. Raiford, T. S.: Tumors of the Small Intestine, Arch. Surg. **25**:122 (July), 321 (Aug.) 1932.

3. Schottenfeld, L. E.: Lipomas of the Gastrointestinal Tract, Surgery **14**:47-72 (July) 1943.

Physical examination revealed a well-developed, moderately obese, well-preserved, elderly woman complaining of lower abdominal pain and tenderness in the right lower quadrant. Her blood pressure was 140/80, pulse rate 86, and respiratory rate 20. Examination of the abdomen showed it to be moderately distended and to be tender in the right lower quadrant. No muscle spasm and no palpable abdominal mass or viscera were present. The pelvic region was normal.

The laboratory examination showed 4,500,000 red blood cells, a hemoglobin content of 13 gm. per 100 cc., and 6,450 white blood cells, with a normal differential count. The urine was normal except for the presence of rare granular casts. The feces did not contain blood, ova or parasites, and the Wassermann reaction was negative.

The patient was operated on, a preoperative diagnosis of acute intestinal obstruction, etiology undetermined, having been made. At operation a moderate amount of straw-colored, nonodorous fluid was present in the peritoneal cavity. A mass was palpated in the cecum, but there were no lymph nodes in the mesentery, and the examination of the rest of the abdominal contents showed no evidence of metastatic tumor. It was first thought that a carcinoma of the cecum was present, and after preparation of the transverse colon for ileocolostomy the tumor was reinvestigated and a typical intussusception into the cecum was found. The intussusception was easily reduced, and a mass estimated to be 10 cm. long could be palpated in the distal ileum. Segmental resection of the ileum with adequate uninvolved bowel wall on each side of the tumor was done, and a primary end-to-end anastomosis was performed. The abdominal cavity was closed, a Chaffin sump drain being left in the right lower quadrant. The patient received 1,000 cc. of whole blood during and immediately after the operative procedure.

The sump drain worked satisfactorily during the postoperative period, and it was removed in approximately 48 hours. The postoperative convalescence was entirely uneventful until the tenth postoperative day, when she began to have a low-grade fever and tenderness in the region of the lateral malleolus of the left leg and in the sole of the left foot. Twenty-four hours later she had pain in the right side of her chest associated with depressed breath sounds and moist rales. Roentgenologic examination showed consolidation in this area. It was thought that she had thrombophlebitis and a small pulmonary infarction in the right side of the chest. Conservative therapy resulted in complete recovery. On Aug. 3, 1950, she was discharged, with no complaints and with the abdominal wall well healed.

To summarize, treatment of lipoma of the ileum consists in (1) reduction of the intussusception followed by enterotomy and excision of the tumor and closure of the bowel transversely, (2) reduction of the intussusception followed by segmental resection and end-to-end anastomosis of the bowel containing the tumor, or (3) resection of the entire bowel involved when it is impossible to reduce the intussusception.

SUMMARY

A case of lipoma of the ileum resulting in recurrent abdominal pain and acute intussusception is presented. Reduction and segmental resection of the portion of bowel containing the tumor were performed.

OLLIER'S DISEASE

JAMES A. HECKMAN, M.D.
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OLLIER first described, in 1900, a rather rare condition characterized by multiple areas of unossified cartilage in the metaphyses of long bones. This disease which now bears his name is more aptly called multiple enchondromatosis and is actually a dyschondroplasia as it is due to a developmental error in endochondral ossification.

According to Fairbank[1] the lesions of enchondromatosis have a tendency for unilateral distribution, with involvement of one bone or several bones of one extremity. Two lower limbs may be affected, and only rarely are all four extremities involved. Enchondromas of the bones of the hands are rather common. The commonest site is in the metaphyseal region of long bones; however, the pelvis is a favorite site. The skull, sternum, ribs, and vertebral column are only rarely involved.

Shortening of the involved limb is characteristic, and Fairbank reports a case of an 18-yr.-old youth with the involved limb 10 in. (25 cm.) shorter than the normal limb. Deformities are common as a result of one half of a metaphysis being occupied by columns of unossified cartilage cells and thus retarding growth in the corresponding epiphysis. Fractures of the involved limb are said to be uncommon. The roentgenological appearance is rather characteristic, with large areas of cartilage cells arranged in columns in the metaphyseal regions. The diaphyses are rarely involved. The density of bone between the cartilage columns is often increased. Blood calcium, phosphorus, and phosphatase studies yield normal results.

In the differential diagnosis this disease is occasionally confused with Albright's syndrome. Diaphyseal aclasia and osteopoikilosis should not be particularly difficult to differentiate. Maffucci's syndrome is a condition in which dyschondroplasia is associated with hemangiomas. Osteogenesis imperfecta must also be considered in the differential diagnosis.

The following case is presented as a typical example of Ollier's disease:

D. A. D., a 10-year-old white girl, was first seen at her home on March 6, 1949, approximately three hours after she fell down a flight of stairs, sustaining a fracture of the right femur. When the child was seen she was lying on the stairs complaining of severe pain in the right leg and did not allow anyone to move her. She had been crippled for many years and had been treated elsewhere for "tumors" of the right leg since she was a small child.

Physical examination with the child lying on the stairs revealed an evident fracture of the right femur. In addition, there was noted a marked shortening of the right leg, with a deformity of the right lower extremity amounting to a "C" curve just above the ankle. The leg was splinted, and the child was taken to St. Mary's Hospital, where roentgenograms revealed an oblique fracture through the midshaft of the right femur, with minimal displacement. In addition,

1. Fairbank, T. H. A.: Ollier's Disease: Multiple Enchondromata, J. Bone & Joint Surg. **30-B**(No. 4):689-704 (Nov.) 1948.

multiple cystic areas of both the proximal and the distal third of the femur as well as the superior pubic ramus were noted. After roentgenologic examination and with the child under general anesthesia the right leg was immobilized in a double hip spica. Roentgenograms showed the fracture to be maintained in good alignment. Further roentgen examination on March 7, 1949, revealed cyst-like lesions involving the metaphyseal regions of the tibia. Laboratory studies revealed a calcium level of 8.9 mg. per 100 cc., phosphorus 6.9 mg., and alkaline phosphatase 4.5 Bodansky units.

Fig. 1

Fig 2

Fig. 1.—Roentgenogram shows the healing oblique fracture in the shaft of the right femur with the enchondromas in both the proximal and distal metaphyseal regions.

Fig. 2.—Roentgenogram of right femur showing healed fracture.

Complete physical examination revealed no abnormalities, other than those noted above, with the exception of a large hairy pigmented area on the posterior aspect of the left arm just above the elbow joint. The patient was discharged on March 10, 1949, and was readmitted on April 10 at which time the cast was changed, a long leg cast being applied. Roentgen reexamination showed almost complete obliteration of the fracture line. The child was then seen on several occasions until the cast was finally removed on May 23, when roentgenograms showed complete healing of the femur fracture. After complete healing of the femur fracture the question arose as to how she could best be rehabilitated so far as the involved leg was concerned.

Physical examination at this time revealed the obvious deformity just above the right ankle, with the right leg approximately 6 in. (15 cm.) shorter than the left. At this time a supracondylar amputation was recommended as the best method of completely rehabilitating the child, the feeling being that with a well-fitting prosthesis she would be better equipped to face life than with any amount of reconstructive surgery which could be done. She was taken elsewhere for various opinions and received the same recommendation from two well-recognized orthopedic surgeons. She therefore was readmitted to St. Mary's Hospital on June 21, 1949. The red blood cells numbered 3,650,000 and the white blood cells 10,000, and the hemoglobin content was 78% with polymorphonuclear cells amounting to 68%, lymphocytes 30%, and monocytes

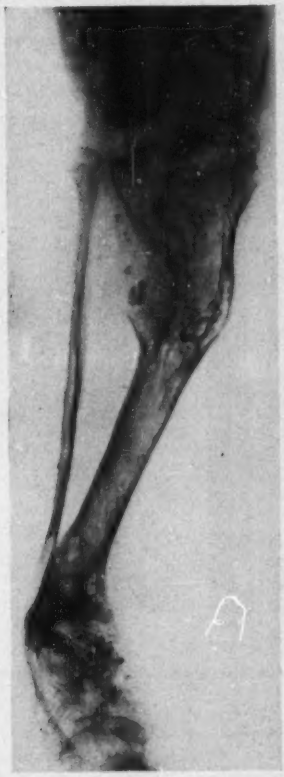


Fig. 3

Fig. 4

Fig. 3.—Roentgenogram of right tibia and fibula showing the characteristic lesions along with the deformity and shortening.

Fig. 4.—Gross appearance of the amputation specimen after the soft tissue was dissected free. Note deformity.

2%. The urine was entirely normal. Survey roentgenograms of the entire right leg showed a complete union of the fracture through the shaft of the femur, and once again the characteristic cyst-like bone lesions were recognized. Survey roentgenograms of other extremities showed no evidence of lesions.

On June 22, 1949, the right leg was amputated in the supracondylar region, with the patient receiving a transfusion of 500 cc. of whole blood during the operative procedure. She made an uneventful recovery and was discharged from the hospital on July 1. The stump healed per primam, and when the child was last seen it was fitted with a prosthesis.

The following pathological report was submitted by Dr. W. S. Werthammer, pathologist for St. Mary's Hospital, Huntington, W. Va.:

"The specimen consists of the left tibia and fibula, the distal portion of the femur measuring 9 cm. in length and the patella. Tibia and fibula measure about 30 cm. in length. The tibia is greatly deformed, showing nodular swelling in the proximal and distal metaphysis. Its diameter near the knee joint is 5 cm. and near the ankle joint 4 cm. The tuberositas tibiae is irregular and knobby. The epiphyseal cartilage is irregular. Throughout the proximal marrow cavity

Fig. 5.—Sectioned gross specimen showing the clear islands of cartilage in the metaphyses, with absence of normal medullary canal.

irregularly outlined cartilaginous areas are seen, the largest one measuring about 3 by 1 cm. The distal end of the tibia shows cartilaginous inclusions extending through the entire medullary canal. Over these lesions the cortical bone appears atrophic. The fibula is bent and atrophic where it passes over the distal swelling of the tibia. The knee joint, patella and distal femur appear unchanged.

"Sections show the lesions in the tibia made up of neoplastic cartilage with irregular cells and vascularization. In places, mucinous degeneration is seen. The compact bone near the lesions is atrophic and in places irregularly thickened, very likely due to previous fractures. The bone marrow surrounding the lesions appears fibrotic.

"The diagnosis is multiple enchondromas of the tibia (Ollier's disease)."

The child has made an excellent psychological adjustment to her disability, and her parents state that she is now much happier than at any time in her life. She has obviously gained many pounds in weight. She has reentered public school and is apparently doing well with her studies.

COMMENT

This case represents a classical example of Ollier's disease with unilateral development of multiple enchondromas in the metaphyseal regions of the long bones of one extremity as well as a lesion in the pelvis. In addition, the deformity and shortening of an extremity which have been described by Fairbank are present in this case and represent the underlying problem for consideration in the rehabilitation of the child.

Since amputation was decided on we have been fortunate in obtaining a rare anatomical specimen for study and preservation. Even if the deformity could have been corrected by osteotomy, it is felt that amputation was indicated in view of the marked shortening. The excellent psychological as well as physical adjustment of the child to society justifies our decision.

Surgical Clinics

CONGENITAL HEART DISEASE

COLLEGE OF PHYSICIANS AND SURGEONS
NEW YORK

A clinic on congenital heart disease was held at 11:30 a. m. on Saturday, Dec. 9, 1950, at the College of Physicians and Surgeons, Dr. George H. Humphreys II, presiding.

DR. GEORGE H. HUMPHREYS: The subject for today's discussion is congenital cyanotic heart disease. I should like to present this boy, Edgar Leary, who represents the problem that we are to discuss.

Edgar was referred to our clinic from another hospital in July, 1947, at the age of 11. He has been cyanotic ever since the age of 1 year, when he was adopted, and probably before that. His family history is unknown but he has a brother who has been consistently larger and stronger than he, although about a year and a half younger. The brother also has a heart murmur. Edgar has always been small, but his development has not been delayed, up to puberty. He is now 15 years old and he has not yet shown signs of maturity.

Exertion has always caused considerable dyspnea and deepening of his constant cyanosis, but as time has gone on he has improved somewhat. During babyhood and early childhood his color was extremely dark and he was limited in his activity. As time has gone on, he has been able to do more and more, so that he now walks about a mile to school and he plays some games, including basketball and football, although when he does so he is likely to become dark in color. He has found his limitations and stops when he is out of breath but soon catches up and is able to go on.

He was admitted to the hospital in March, 1948. His appearance at that time was much the same as it is now. He had cyanotic and clubbed fingers, as he has now. As you see, his lips and tongue are moderately cyanotic at rest, but when he exercises the color becomes much darker. Those of you who are close enough can see that his conjunctivas are suffused, which is also a characteristic finding.

Dr. Rogers has his apparatus here for recording the heart murmur, which will permit us to listen to his heart. There is a harsh systolic murmur, and you can hear that the sound of valvular closure is marked. Now, Dr. Rogers, if you can turn the volume a little louder and then move it across gradually, what I should like to emphasize is that one hears a valvular closure in what would ordinarily be considered the pulmonary area, and as one moves away from that point in all directions the sound does not change but simply becomes less distinct; in other words, we hear essentially the closure of a single valve.

The roentgenogram of his heart shows a cardiac contour which is not outside the limits of normal. No diagnosis could be made from the roentgenograms alone. He has evidence of increased vascular marking in his lungs, or at least they are certainly not decreased, and it is sometimes uncertain whether the markings are due to respiratory difficulty or to vascular difficulty. It was uncertain in his case. We determined the blood count in 1948, and it is probably about the same now—19 gm. of hemoglobin, 6,500,000 red blood cells, and hematocrit value of 76%. The electrocardiogram shows left ventricular hypertrophy.

I asked Edgar to come here because he has, we believe, what one might consider embryologically the most primitive form of anomaly resulting in cyanosis. We think that he has a common truncus arteriosus and that the blood which leaves his right and left ventricles is mixed. We know from catheterization that the blood leaving the right ventricle is the same in its arterial content as that in his peripheral arteries and we therefore believe that his condition probably represents the most primitive stage of cardiac differentiation, when the blood entering the heart leaves it through a common vessel, the truncus arteriosus, and goes throughout the arteries of the body as a mixture of arterial and venous blood. This situation normally is present only in the very earliest stages of embryonic life, after which the truncus arteriosus differentiates into aorta and pulmonary artery.

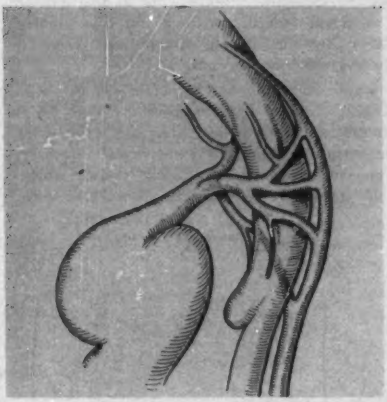


Fig. 1.—Diagrammatic left oblique view of the heart and great vessels in a 7 mm. embryo. (From Humphreys, G. H., II: Surgery of Congenital Anomalies of the Heart and Great Vessels, in Advances in Surgery, New York, Interscience Publishers, Inc., 1949, Vol. 11.)

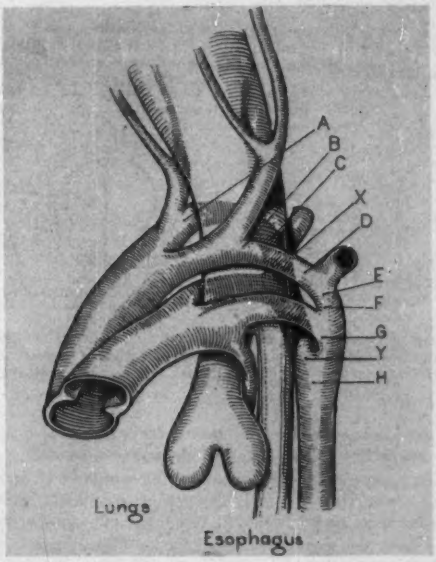


Fig. 2.—Diagrammatic left oblique view of the great vessels in a 12 mm. embryo. (Same reference as that for Fig. 1.)

It is this differentiation of the primitive truncus which causes the anomalies which we see most commonly resulting in cyanosis. Figure 1 is a diagrammatic drawing showing the primitive heart with a common truncus, dividing into the branchial arches, of which the fourth and sixth are shown, the fifth having disappeared. The sixth arch will give rise to the pulmonary artery as it grows into the lung bud.

At a slightly later stage of differentiation, again drawn diagrammatically, we have a situation like that in Figure 2. The fourth arches are now beginning to form the aortic arches, and the sixth arches are forming the pulmonary vessels, with what will become the ductus arteriosus, at this stage a bilaterally symmetrical structure. The common trunk is differentiating, by the growth of spirally developing ridges, which will eventually meet in the midline and divide the trunk into two vessels. When that takes place, the down growth

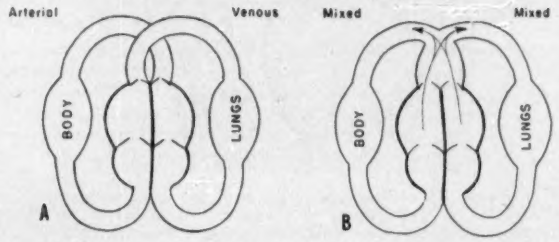


Fig. 3.—*A*, diagram of normal circulation after birth; *B*, diagram of circulation in a case of truncus arteriosus communis.

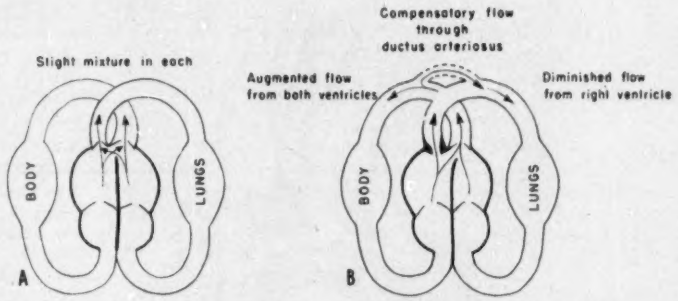


Fig. 4.—*A*, diagram of circulation in a case of high interventricular septal defect with overriding aorta. *B*, diagram of circulation as in *A*, with pulmonary stenosis in addition (tetralogy of Fallot). The compensatory effect of a patent ductus arteriosus is indicated by vessel in broken line.

of the ridges meets the upward growh of the ventricular septum and finally separates the two ventricles and forms the valves of the aorta and the pulmonary artery.

A diagrammatic representation of the normal condition after birth is shown in Figure 3*A*. Obviously, the blood comes from the body into the right auricle, goes through the right ventricle and out into the lungs, back into the left auricle and left ventricle and back into the body.

The boy whom we have just seen had the condition shown in Figure 3*B*. He had a common truncus arteriosus, and the blood which went into the pulmonary artery was the same as that which went into the aorta. However, he can increase his cardiac output and can meet the demands of exertion within limits because there is no block anywhere and no shunting. The circulation through his lungs is equal to that through his body, and he gets along well.

If, on the other hand, this differentiation takes place in a different way and the septum growing downward fails to meet the ventricular septum, particularly if it goes off center so that

it comes over in some such manner as that in Figure 4*A*, then the blood entering the right ventricle will have a choice. It has more or less difficulty in going through the pulmonary artery because this opening is smaller than the aortic opening, and some of the blood entering the right ventricle will go into the lung but some of it will cross over and mix with the arterial blood entering the systemic circulation. In that way, cyanosis will occur through mixing, but it will be a differential shunt. There will be a greater amount of blood going through the peripheral circulation than there will be going through the pulmonary circulation. This may be augmented by a considerable over-riding or by a stenosis in the infundibular area of the right ventricle, which occasionally may be extremely tight, so that the great bulk of the blood goes through into the left heart (Fig. 4*B*).

On the other hand, the differentiation may take place normally but may be incomplete. There may be a simple defect in this area (Fig. 5*A*), in which case the greater pressure on

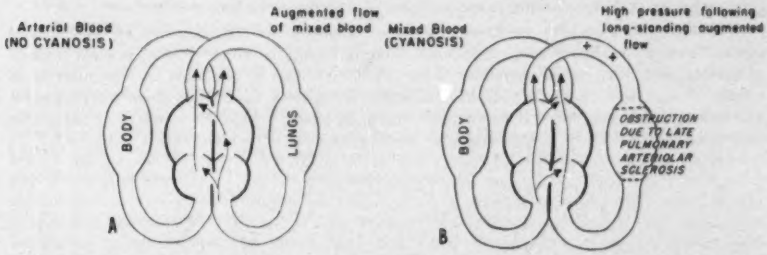


Fig. 5.—*A*, diagram of circulation in a case of high interventricular septal defect without over-riding aorta. An interatrial septal defect is also indicated. *B*, diagram of circulation as in *A* after pulmonary vascular changes have resulted in increased resistance to pulmonary flow.

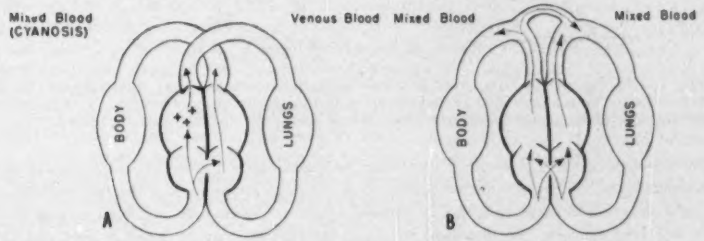


Fig. 6.—*A*, diagram of circulation in a case of pulmonary valvular stenosis with interatrial septal defect; *B*, diagram of circulation in a case of transposition of the great vessels, with interatrial septal defect and patent ductus arteriosus functioning as compensatory anomalies.

the left will tend to push blood over into the right and there will be no cyanosis unless in a late stage the resistance in the lungs through changes in the pulmonary vessels finally causes a heightened pressure here which then shifts the shunt the other way (Fig. 5*B*).

Finally, the differentiation may be normal except for the valves themselves. If the valve which forms at the very end of the differentiation of the truncus becomes stenotic, with a normal septum, the foramen ovale, which is a normal fetal structure, may remain open because of the back pressure which develops in the right ventricle and auricle and blood keeps flowing from the right to the left through the auricular septum. This results in pulmonary valvular stenosis. It may occur in pure form without a patent foramen ovale, but more commonly there is an auricular opening and occasionally also a ventricular opening, which allows a right-to-left shunt and hence, cyanosis (Fig. 6*A*).

Occasionally, of course, there is a reverse differentiation, or so-called transposition of the great vessels, a condition obviously incompatible with life, unless there is some means of getting the venous blood through the lungs. This may take the form of a large patency in the auricular septum, or it may take the form of a persistent patency of the ductus arteriosus which allows venous blood to enter the lungs in that fashion. In either case, venous blood will be mixed with arterial blood in the lungs, and, similarly, there will be some cross-over and mixing of arterial blood in the body, but this results in profound cyanosis (Fig. 6*B*).

These observations concern the lesions of the truncus arteriosus. There are a few other lesions within the heart itself which also result in cyanosis and which should be mentioned, since they must be differentiated from the truncus lesions which form the best group for surgical intervention. The one that is most easily understood is a large ventricular septal defect, a so-called three-chambered heart, in which blood mixes freely from both auricles and passes out into both great vessels in an approximately equal mixture. This condition may vary a great deal according to the level and size of the septal defect (Fig. 7*A*).

The other lesions which we have seen more commonly are the anomalies of the tricuspid valve. When the tricuspid valve is stenotic, there is usually a failure of the auricular septum to develop, and there may be a failure of the whole right side of the heart, so that there is an atresia of the right ventricle and the pulmonary artery and all the blood goes through the left heart. Here again there is a profound mixing of blood, a situation which is not amenable to surgical correction. A ductus arterious would neutralize it to some extent (Fig. 7*B*).

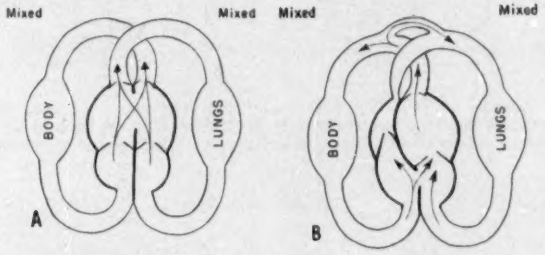


Fig. 7.—*A*, diagram of circulation in a case of large interventricular septal defect. *B*, diagram of circulation in a case of tricuspid atresia with hypoplasia of right ventricle and pulmonary artery and interatrial septal defect. A compensatory patent ductus arteriosus is shown.

On the other hand, the tricuspid valve may be inadequately formed and may remain as an incompetent valve which dilates and allows blood to regurgitate so that the two auricles and the right ventricle become, in effect, a common chamber, again with profound mixing in the heart and deep cyanosis. In this case, the auricular opening may be small at first and there may be relatively little cyanosis until, with dilatation of the auricles, the opening becomes large and an increasing right-to-left shunt occurs.

This is a brief sketch of some of the embryologic and anatomic considerations. I will now ask Dr. Richards to discuss the physiological implications of these mechanical changes.

Dr. Dickinson W. Richards: The possibility of cyanosis in congenital heart disease depends first of all on a false communication between the venous and arterial sides of the circulation, short-circuiting the lungs. It may occur at various points in the pulmonary and systemic circuits. Perhaps the simplest is the pulmonary arteriovenous aneurysm, hemangioma of the lung, a rare condition but a simple one physiologically, since blood moves directly from the pulmonary arteries to the pulmonary veins without being aerated in the alveoli. At the other end of the system of great vessels, one occasionally sees a communication between the superior vena cava and the pulmonary vein. Another fairly simple communication, which Dr. Humphreys has mentioned, is the interauricular, the open patent foramen ovale, about which I shall speak further later. Then there are the various more complex intracardiac forms, which Dr. Humphreys has just presented and which I shall not review again.

These considerations have to do with the possibility of the development of cyanotic heart disease. Whether cyanosis will develop and to what extent depends, of course, on the size of the communication and the relative pressures on the two sides. If there is much pressure difference, the type and amount of flow across the false passage is apt to remain relatively constant; thus, in the pulmonary hemangioma which I just mentioned, the mean arterial pressure being in the region of 15 mm. and the mean venous pressure being in the region of 4 or 5 mm., there is a direct right-to-left communication of an amount depending on the size of the lesion and cyanosis is always present.

On the other end of the scale, there is the patent ductus arteriosus, in which, with much pressure in the systemic aorta and little pressure in the pulmonary artery, the flow is wholly left to right and there is no cyanosis. The chief dynamic effect there, of course, is an increased flow through the pulmonary vascular bed by reason of the double in-flow from patent ductus and from pulmonary artery.

When the pressures on the two sides are not greatly different, especially if the opening is a large one, small alterations in dynamics on the two sides may cause great variations in cyanosis. An interauricular septal defect, for example, is responsible for a small degree of cyanosis due to right-to-left shunt, even in the resting condition. This comes about by way of the slight differences in pressure on the two sides. In the right auricle, the pressures during the entire cardiac cycle change but little, perhaps from —3 to +2 mm. of mercury, with a mean level around 0. In the left auricle, the mean pressure is about 3 or 4 mm. higher, but here there are also wider swings in pressure through the cardiac cycle, due to the fact that the volume capacity of the pulmonary blood bed and the left auricle is small, relative to that of the systemic great veins and the right auricle. Twice during the cardiac cycle, that is, during the "descent of the base" of the heart early in ventricular systole and again with ventricular relaxation and opening of the mitral valve, the pressure in the left auricle falls sharply and becomes lower than the pressure in the right auricle.

Thus it comes about that while most of the flow in auricular septal defect is from left to right, there is also a small component of right-to-left flow, enough to decrease the arterial blood oxygen saturation to about 92 or 90% from the normal 96%.

In situations of this kind, in which the pressures are not greatly different on the two sides, physiological events will shift the relative flow from one side to the other to a considerable degree. Exercise, for example, which may increase the venous pressure considerably on the systemic side, may cause further increases in flow to go from right to left. Crying in infants will do the same thing.

From a somewhat different cause but on the same principle, when the total flow has to increase, as in muscular exercises, in cases in which pulmonary in-flow is reduced by means of a narrow passage (pulmonic stenosis or tetralogy), and in which there is a larger false passage, a larger fraction of the blood tends to go through the wider pa[illegible] and a relatively smaller flow through the narrow passage, in this case the pulmonic stenosis. The lungs get relatively less blood therefore, and again cyanosis increases.

Somewhat less common but nonetheless an important feature at times may be a sudden lowering of pressure on the systemic side of the circulation, which may affect both the left ventricular filling and the left auricular pressure, causing it to be less and tending to produce, therefore, larger amounts of right-sided blood flow into the left side on that account.

This much relates to immediate changes due to physiological events from moment to moment. There is also in many, or perhaps most, of these cases a natural history, a progression over the years, which may change substantially the amount of cyanosis. Factors tending to increase pressure on the right side of the heart are numerous. Perhaps the most important is the gradual development of pulmonary arteriosclerosis.

As you know, this condition appears to be favored by long-standing increases in flow through the pulmonary vascular channels. It certainly is favored by long-standing increases in pressure in these channels. Thus, pulmonary hypertension tends to build itself up through the development of arteriosclerosis over the years, even in relatively young persons, if the lesion is a severe one, and this will tend to increase the right-sided pressure and therefore the flow from right to left in congenital heart disease. It will also lead to right ventricular dilatation and failure and total congestive failure on the right side.

Pulmonic stenosis itself is a lesion which often progresses and becomes severer with increased scarring and narrowing; so do others of the congenital anomalies that have already been mentioned. Therefore, as the years go on, the cyanosis in many of these cases tends to increase.

The development of marked cyanosis late in the clinical course of a patient with a congenital heart lesion is often referred to by the French term "cyanose tardive." I have a patient, now 50 years of age, whom I have followed for ten years and who has a pronounced interauricular septal defect with associated aneurysmal dilatation of both pulmonary arteries. He has had slight to moderate cyanosis, some polycythemia, and exertional dyspnea, but without congestive failure. During the past year, however, he has had several episodes, usually following exertion or emotional episodes, when he suddenly became intensely cyanotic, felt dizzy, and then lost consciousness. Examination at these times has shown increased venous pressure and all the signs of acute right heart failure. Evidently these episodes are caused by acute right ventricular failure, increased right auricular pressure, and sudden pouring of venous blood through the auricular septal defect directly into the left auricle.

These are the main points that I should like to bring out. There are secondary effects, of course, and I might mention two of them. Polycythemia, as we see it, seems to be a phenomenon developing with continuous arterial anoxia and cyanosis. The patients with intermittent anoxia have relatively little tendency to polycythemia or the attending increase in blood volume.

The condition to be finally discussed is respiratory gas exchange in persons with reduced pulmonary blood flow. There is in this situation a considerable physiological problem for the body to eliminate enough carbon dioxide and to absorb enough oxygen when so small an amount of blood, relatively, passes through the pulmonary vascular bed. This has to be accomplished by marked hyperventilation, which is regularly seen and by means of which the patient is able to extract 9 or 10 cc. of carbon dioxide for 100 cc. of blood flowing, as compared with the normal 4 cc. per 100 cc., and to put into the much reduced blood that comes into the pulmonary vascular bed some 10 cc. of oxygen or more. In other words, the arteriovenous difference can be increased through the simple means of hyperventilation. However, hyperventilation also means that the reserve that these patients have for any additional stress is greatly reduced and their exercise tolerance is, of course, minimal.

DR. HUMPHREYS: These anatomical and physiological disturbances were interesting to anatomists and physiologists but not particularly so to cardiologists and not at all interesting to surgeons until about five years ago, when it was realized that if compensating shunts could be made the cyanosis of some of these conditions could be relieved. For this reason, it is now important to study each case with great care, not only to discover whether the particular lesion is one amenable to surgery but also to find out in general what is going on, so that we can learn more about the varied conditions and perhaps approach new problems of therapy.

Hardly two of these patients have identical anomalies. The fact that we classify them into categories and give them the names of the persons who first described them in general does not mean that they are distinct entities. They fall into clinical groups. Tetralogy of Fallot, for example, is one that has been emphasized, since it was the first to be treated surgically. However, the physiological changes that occur in tetralogy of Fallot vary widely, and they vary all the way into lesions of other types.

We are getting away now from classification by name and are beginning to think more in terms of types of physiological disturbances rather than of purely anatomical pigeonholing according to categories.

In making a diagnosis, we rely primarily on the electrocardiograph, the roentgenogram, and, especially, cardiac catheterization. The electrocardiograph tells us little except whether the right or the left heart is working the harder. The roentgenogram tells us somewhat more, and the cardiac catheterization tells us the most.

I shall ask Dr. Caffey, first, to discuss the roentgenologic signs.

DR. JOHN P. CAFFEY: Dr. Humphreys has already put the roentgenogram in its proper place, as being of secondary or tertiary value, and that is important because many of the mistakes in the use of roentgenograms are made because it is assumed that the findings are specific.

Probably more has been learned about the roentgen shadows in congenital heart disease during the last five years than in all the earlier studies, because now cases are being examined and the diagnosis is being proved. As Dr. Humphreys has indicated, the most important thing that has been found is the high frequency of variations in the same lesion. For example, Dr. Richards described a patient with extreme cardiac and pulmonary artery malformation, with interauricular septal defect. Actually, there are probably many interauricular septal defects that do not deform the heart or the pulmonary arteries at all.

Dr. Dexter and his group in Boston showed this with catheterization; so that we now know that perhaps 75 or 80% of the patients who have congenital lesions do not present the extreme characteristic type of shadows that have been used in diagnosis. That has an important implication because it means that roentgenograms can never be used to exclude a lesion like patent ductus arteriosus or interatrial septal defect. We do not yet know, although the information is accumulating rapidly now, how many cases are typical and how many are atypical. I think probably 15% or fewer cases will show all the classical signs we used to demand for the diagnosis of these lesions.

Therefore roentgen findings are supplemental, particularly to catheterization, which provides information which cannot be got by the roentgen method. It always bears repeating that the roentgen findings alone are often misleading unless they are closely correlated with all the other findings. Sometimes, for example, the history is more characteristic and diagnostic in tetralogy of Fallot than the roentgen findings are, and frequently we have seen patients with proved patent ductus arteriosus which has been ligated in whom there were no changes in the heart or the pulmonary circulation visible roentgenographically, either before or after the procedure.

The time of greatest error in diagnosis, undoubtedly, is during the first months or weeks of life, and all the students here, particularly, should realize that the cardiac shadow is not stabilized for several weeks after birth. When the heart is cut off from the placental circulation at birth, it is still dilated, and in some infants it takes as long as two or three months for the heart shadow to shrink to its normal size. We have seen several patients in whom there were large cardiac shadows by ordinary standards, murmurs, and transient or sometimes continuous cyanosis, all three of which manifestations disappeared during the first month and later the children were normal. It is important that the diagnosis in congenital heart disease be considered undecided even though there are pronounced clinical and roentgen signs, until after this period of adjustment which occurs in the first weeks of life and which takes longer in some patients than in others. I prefer to wait for six months before a conclusive diagnosis is made. You will save parents a great deal of anguish and unnecessary torture from worrying about heart disease if the diagnosis during the first months is kept in abeyance until conclusive signs appear.

When should the patient be subjected to the procedures, some of which are hazardous, of angiocardiography, catheterization, and electrocardiography? In every clinic one of the outstanding features of surgical treatment is that the younger the patients treated the greater the mortality. That is true here, is it not?

DR. HUMPHREYS: Yes.

DR. CAFFEY: Many needless angiocardiographic studies of infants who are not going to be treated surgically until the third or fourth year are done during the first and second years. The surgeon would rather have the examination as near the operation as possible, when the information is most valuable, and so we do little but conventional investigation during the first months or first years but wait until surgical treatment is anticipated.

There are some exceptions to this rule, of course, and the outstanding ones are the congenital anomalies of the aorta. If they are causing compression symptoms of the respiratory tract, patients are examined early and completely; surgical treatment is often urgent. When the blood count shows more than 8,500,000 red cells, the frequency of intracranial thrombosis is so high that it is hazardous to postpone operation. In cases of heart failure in congenital heart disease operations are sometimes done early at great risk although the prognosis is bad. In general, the definitive investigation of congenital malformation of the heart should be postponed until the third or, better, the fourth year.

It is also well to keep in mind that the typical cases of patent ductus arteriosus or coarctation of the aorta and of Fallot's tetrad can be diagnosed almost conclusively from the history, physical examination, and fluoroscopy. It is the unusual case that requires elaborate investigation.

There is one use of the aortogram in coarctation that should be mentioned. Dr. Gross, in doing his repair operation or graft operation, uses the aortogram to give a better estimate of the size of graft to use, the exact location and the length of the stenosed segment. If surgical treatment is anticipated, an aortogram and not an intravenous injection of dye is needed, because after the dye goes through the lungs it never assembles again in good concentration and often, even with the best technique, the aorta is not clearly visualized and accurate measurement cannot be made of the length of the stenosis in the aorta.

Many of the cases of coarctation show no deformity of the external surface of the aorta even when the lumen is stenosed to almost a pinpoint, but there is a compensatory local thickening of the wall, so that in a fluoroscopic view of the outside of the aorta the stenosis would not be evident. Therefore, it is often not possible to see coarctation of the aorta fluoroscopically. I have never seen narrowing in the shadow of the aorta fluoroscopically in a child.

It should be mentioned that with the techniques which we now use the patent ductus itself is rarely visualized in patent ductus arteriosus, and the only place I have actually seen the ductus is on retrograde aortograms. In addition to the patent ductus, there are sometimes anomalous vessels that interfere with the surgical treatment, particularly of coarctation, and aortograms furnish evidence of that kind which cannot be obtained in any other way.

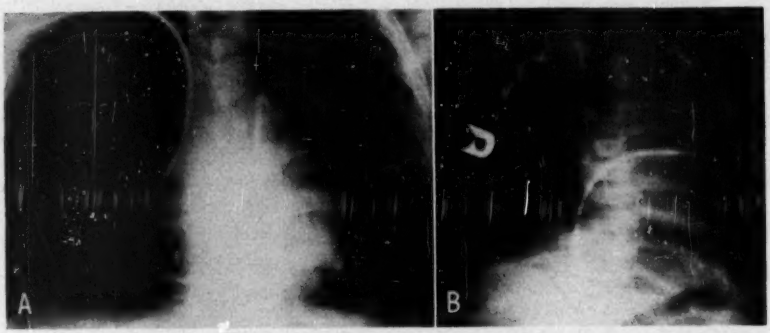


Fig. 8.—*A*, roentgenogram showing intracardiac catheter with tip in pulmonary artery. *B*, roentgenogram showing intracardiac catheter with tip crossing from right to left auricle through an interatrial septal defect to enter a left pulmonary vein.

The most interesting lesion from a roentgenologic standpoint at the present time is solitary pulmonary stenosis, which roentgenologists have overlooked for years. It is a lesion best demonstrated by catheterization, and it presents the peculiar paradox that beyond the stenosis there may be dilatation with, according to Dr. Sosman, excessive pulsation.

These are some of the important recent trends. The most important single structure from the standpoint of roentgen diagnosis is the pulmonary artery, and both its smallness and largeness enter into the diagnosis. The pulmonary artery may be large and conspicuous in persons who are longitudinal in type, since the arteries project farther from a narrow mediastinum than they do from a wide one. The differentiation of idiopathic dilatation of the pulmonary arteries from large normal pulmonary arteries becomes a roentgenologic problem. The clinical history and the other findings must be the deciding factors in estimating the significance of these shadows.

DR. HUMPHREYS: The assistance afforded by information obtained through cardiac catheterization is outstanding in these cases, and I will ask Dr. West to discuss briefly the approach along those lines.

DR. JOHN R. WEST: The establishment of anatomic diagnosis of congenital heart disease by cardiac catheterization depends on the evaluation of three kinds of data obtained by this procedure. These are (1) the positions taken by the catheter during the procedure, (2) the pressures recorded within the heart and great vessels, and (3) the oxygen content of the blood samples which are withdrawn from the various chambers.

Sometimes the position or course taken by the catheter is sufficient to establish an anatomic diagnosis, sometimes the pressure findings are all that are required, and sometimes the diagnosis rests solely on the analysis of blood samples. Usually, however, one must consider all the findings together before any reasonable conclusion can be made.

For the purpose of today's discussion, I intend to present data on catheter positions, intracardiac pressures, and intracardiac blood samples separately and then to discuss the data obtained by catheterization in three illustrative cases.

My first slide shows the catheter as it appears on roentgen examination when the tip lies in the left pulmonary artery (Fig. 8*A*). You can see the instrument in the superior vena cava and the right auricle. In the right ventricle the detail is poor because of catheter motion while the roentgenograms was taken. You can see the instrument again, however, in the main pulmonary artery and in the left branch. From this slide the appearance of the instrument can easily be visualized when the tip lies in the various chambers of the right heart in usual circumstances.

Sometimes the catheter will be passed easily through anomalous openings in the heart. For example, if the catheter is observed to take the position shown in Figure 8*B*, the likelihood is that it has entered the left auricle through a defect in the auricular septum and has gone out

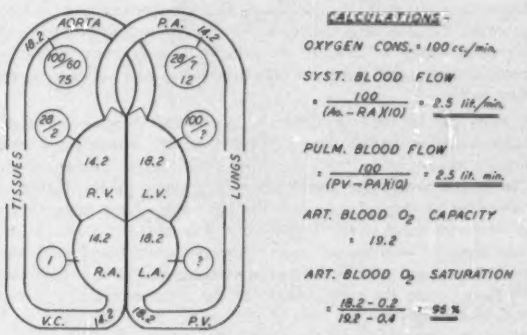


Fig. 9.—Intracardiac pressures and oxygen content in a normal child aged 3.

into a pulmonary vein. To be absolutely certain, a sample of blood must be obtained from this location of the tip which has the oxygen content expected of pulmonary venous blood .

Occasionally in patients with a high interventricular septal defect and over-riding of the aorta, the catheter will be observed to pass from the right auricle into the right ventricle and up and out into the aorta. Sometimes this pathway will be simulated in the case of a large right auricle, the catheter simply making a loop and going back up the superior vena cava. If, however, a blood sample is withdrawn and a pressure tracing is recorded, the exact location of the catheter tip can be determined. If the tip is in the aorta, an aortic pressure tracing will be obtained and the blood sample will have the same oxygen content as one drawn from the brachial artery. If the tip lies in the superior vena cava, a low pressure will be recorded and the blood sample will be low in oxygen.

The next slide refers to intracardiac pressures and to oxygen content of blood in the various chambers in a normal person (Fig. 9). The figures within the chambers indicate the oxygen contents expressed as volumes per cent. The figures in circles outside the various chambers indicate the pressures expressed in millimeters of mercury.

Note that the blood oxygen content is represented as being the same throughout the right heart. Actually this is not the case in most normal persons because blood entering the right auricle comes from the inferior vena cava, superior vena cava, and coronary sinus, all of which have different oxygen contents, and proper mixing of blood possibly does not occur until the blood reaches the right ventricle and probably not until it reaches the pulmonary artery. Further-

more, the method used for determination of oxygen content of any blood sample has certain limitations of accuracy. For these reasons, then, we accept variations in oxygen content of up to 0.6 volumes per cent as within normal range for the various chambers of the right heart.

The pressures in the right heart chambers are lower than those in the corresponding chambers on the left. Normal pulmonary artery pressure is less than 30 mm. systolic, less than 10 mm. diastolic, and less than 15 mm. mean. Normal right ventricular pressure is less than 30 mm. systolic and less than 5 mm. diastolic. Normal right auricular pressure is less than 5 mm. mean.

The diagnosis of some lesions is based on considerations of pressure findings alone. Thus the findings of a right ventricular systolic pressure considerably greater than pulmonary arterial systolic pressure indicates the presence of pulmonic stenosis if right ventricular pressure is abnormally high. If right ventricular systolic pressure is normal yet considerably greater than pulmonary arterial systolic pressure, the diagnosis of idiopathic dilatation of the pulmonary artery must be entertained.

The diagnosis of other lesions is often suggested by pressure findings. Thus, if in a cyanotic person equal systolic pressures are recorded in the right ventricle and the brachial artery, it is likely that there is a high interventricular septal defect with an over-riding aorta, for with this anomaly the right ventricle ejects blood directly into the aorta, and hence right ventricular systolic pressure must be slightly greater than aortic systolic pressure. Of course, in some instances of pure pulmonic stenosis with resultant right ventricular hypertension and cyanosis resulting from patent foramen ovale, the systolic pressures in the brachial artery and the right ventricle may be equal purely as a matter of chance. In general, however, the finding of equal systolic pressures in brachial artery and right ventricle in cyanotic heart disease suggests the presence of an over-riding aorta.

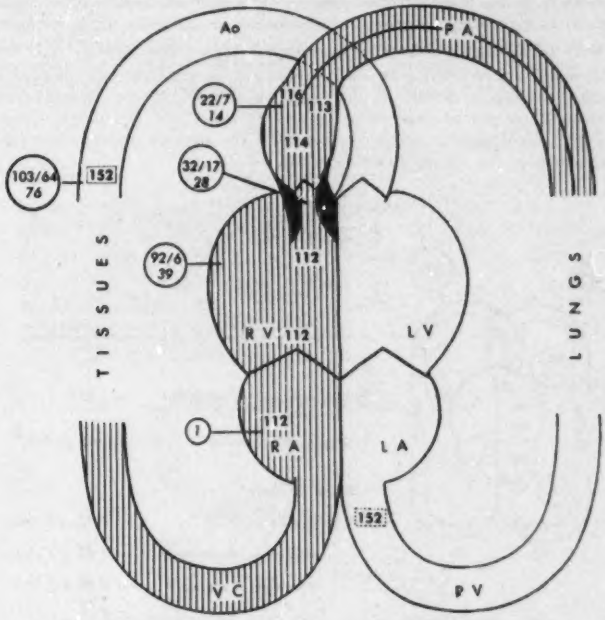
This same slide can be used to illustrate how blood samples are useful in making a diagnosis. The pressures on the left side of the heart, auricle, ventricle and aorta, are uniformly higher than are the pressures on the right side of the heart. Therefore, in the case of an interauricular or an interventricular septal defect or a patent ductus, highly oxygenated blood from the left side will be shunted over into the right side of the heart. For example, in the presence of an interventricular septal defect, you might find that a sample of blood from the right auricle contained 14 volumes per cent of oxygen while blood from the right ventricle and pulmonary artery might contain 16 to 18 volumes per cent. This would indicate that after the blood passes from the right auricle to the right ventricle, it becomes mixed with some arterialized blood from the left side of the heart. The only likely explanation in most instances would be the presence of an interventricular septal defect.

Similarly, if samples of blood from the right ventricle and the right auricle are equal in oxygen content but are lower in this respect than samples of blood from the pulmonary artery, the likelihood is that there is a communication between the aorta and the pulmonary artery. By far the commonest communication of this type is patent ductus arteriosus. A finding of unsaturation in arterial blood in a peripheral artery indicates that in some manner venous blood enters the left side of the circulation. It can enter through an auricular septal defect if right auricular pressure exceeds left auricular pressure or through a high interventricular septal defect with over-riding of the aorta, or, in some rare instances, it can occur in patent ductus arteriosus if there is enough peripheral resistance in the pulmonary vascular bed to elevate the pressure in the pulmonary artery to such a degree that a reversal of flow can occur.

I will give some examples of actual catheterization studies (Fig. 10). Here are the findings in a patient with pure pulmonic stenosis. Note first that there is no arterial unsaturation, arterial blood being 95% saturated. Note that the blood samples obtained from the pulmonary artery, right ventricle and auricle are all more or less the same in oxygen content—116, 119, 114, 112 and 112, expressed as cubic centimeters per liter. Note, however, that the pressure in the pulmonary artery was only between 22/7 and 30/17, while in the right ventricle it was 92/6. This clearly indicates the presence of pulmonic stenosis. The absence of arterial unsaturation indicates the absence of a right-to-left shunt. The absence of arterialization of the blood from the right heart indicates the absence of any significant left-to-right shunt.

A more complex finding is illustrated in Figure 11. This is a case of tetralogy of Fallot. The patient was cyanotic at rest and had evidence of right ventricular hypertrophy on electrocardiograms but no evidence on roentgenologic examination of any cardiac abnormality. On

cardiac catheterization, the following data were found: The oxygen content of the blood from the two venae cavae averaged 15.9 volumes per cent. In the right auricle, it was 15.8, in the right ventricle, near the tricuspid valve, 16, and in the right ventricle, near the outflow tract, 18.2 volumes per cent. From this point, the catheter was easily introduced into the aorta, and there blood containing 19.5 volumes per cent oxygen, identical to that in the brachial artery, was obtained. The arterial saturation was 84 per cent.



Arterial blood oxygen capacity . . . . . = 162 cc/lit.
Arterial blood oxygen saturation . . . . . at rest = 95%
Arterial blood oxygen saturation following mild exercise = 94%
Oxygen consumption . . . . . at rest = 186 cc/min.

ESTIMATED BLOOD FLOW

Systemic (Q_s) . . . . 4.78 lit/min.
Pulmonary ($Q_{p.}$) . . 4.78 lit/min.

Fig. 10.—Catheterization studies in a patient with pulmonic stenosis. (From Cournand, A.; Baldwin, J., and Himmelstein, A.: Cardiac Catheterization in Congenital Heart Disease, London, Commonwealth Fund, 1949, pp. 31, 61 and 62.)

The catheter was withdrawn from the aorta into the right ventricle, and the pressure tracing in Figure 11 was recorded. Note that the aortic systolic level is identical with the right ventricular systolic level.

After the catheter was withdrawn into the right ventricle, it was advanced again, and this time it entered the pulmonary artery, where blood containing 17.0 volumes per cent oxygen was obtained. The pressure recorded in this location was very low, and withdrawal of the

catheter from the area gave a low pressure in the pulmonary artery with a marked increase as soon as the catheter was pulled back into the right ventricle, clearly indicating the presence of pulmonic stenosis.

The peripheral arterial unsaturation indicates the presence of a right-to-left shunt. The rise in oxygen content from 15.8 in the auricle to 18.2 in the right ventricular outflow tract indicates the presence of an interventricular septal defect. The marked difference in pressure between pulmonary artery and right ventricle indicates pulmonary stenosis. The identical systolic pressures in the brachial artery and the right ventricle suggested over-riding of the aorta, and this was confirmed by passage of the catheter into the aorta from the right ventricle.

These were the findings which led us to make the diagnosis of tetralogy of Fallot.

It is important, before arriving at any conclusions with regard to data obtained on cardiac catheterization, to make a careful clinical evaluation of every patient, because often the data that are obtained are not as clear-cut as they are in these last two slides. Often they are conflicting and do not clearly indicate the nature of the anomaly present. In these instances clinical evaluation of the patient is all-important.

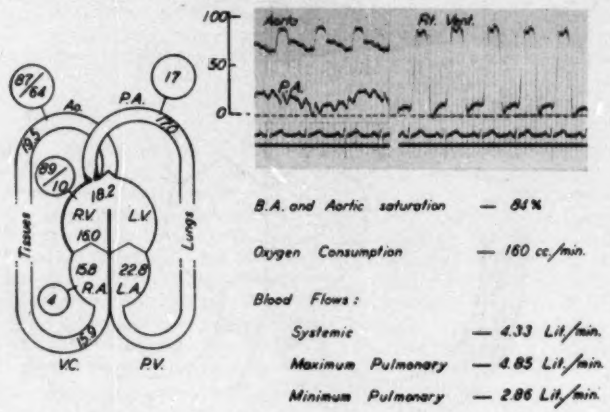


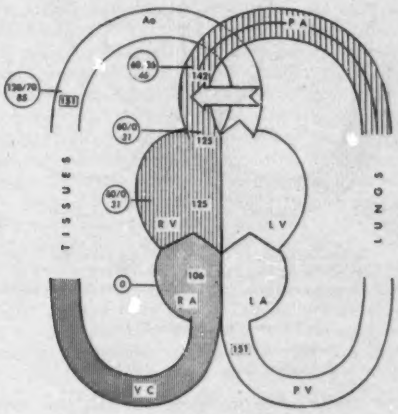
Fig. 11.—Pressure tracing in a case of tetralogy of Fallot.

As an example, I should like to show you two more slides concerning a patient with patent ductus arteriosus. The first slide gives the preoperative findings (Fig. 12). Note that the oxygen content of the blood rose precipitously as the catheter was advanced from right auricle into right ventricle—10.6 to 12.5—but note also that there was an additional rise as the catheter was advanced from the right ventricle into the pulmonary artery, suggesting that in addition to a patent ductus there may well have been an interventricular septal defect. The patient had a loud machinery murmur in the second left intercostal space but did not have a separate systolic murmur below the level of the pulmonic valve, and therefore it was decided that the increase in oxygen saturation in the right ventricle in comparison with the right auricle was due to pulmonic regurgitation secondary to dilatation of the pulmonic valvular ring. This diagnosis was certainly compatible with the high pressures recorded.

Accordingly, the patient was recommended for operation, at which a large ductus was found. Five weeks postoperatively (Fig. 13) the blood oxygen contents throughout the right side of the heart were identical, indicating that there was no longer any shunt. The only abnormality was residual pulmonary hypertension, which had disappeared at the time of a third study performed five months later.

Dr. Humphreys: Dr. West has indicated here the essential differentiation of two of the lesions which are most amenable to surgery, and I will review them just for a second while Dr. McAllister brings in his first patient.

Here, again, we have a crude representation of the type of picture which Dr. West showed us of tetralogy of Fallot (Fig. 4*A*). The basis on which operation is advised is the fact that in the presence of an over-riding aorta, with blood going from the right heart into the aorta and mixing with the blood from the left heart and with an obstruction to pulmonary flow, there is a deflection of blood from the pulmonary circulation into the systemic circuit, so that there is an unequal flow in the lungs as compared with the peripheral circulation. If, then, an artificial ductus arteriosus can be created, this inequality of flow will be neutralized in that some of the excess blood flowing through the aorta will now flow back into the pulmonary circuit and a more equal flow through the lungs and through the body will be created which will eliminate, or nearly eliminate, cyanosis. The flow now coming through from the lungs will be of large volume and can compete successfully with the flow from the right side of the heart. Dr. McAllister's patient presents such a picture.



Arterial blood oxygen capacity . . . . . = 162 cc/lit.
Arterial blood oxygen saturation at rest = 95%
Oxygen consumption . . . . . at rest = 92 cc/min.

ESTIMATED BLOOD FLOW		ESTIMATED BLOOD SHUNT	
Systemic (Q_s)	2.04 lit/min.	Aortico-pulmonary (Y_s)	8.16 lit/min.
Pulmonary (Q_{Pul})	10.20 lit/min.	Pulmonic regurgitation (R) . . .	2.28 lit/min.

Fig. 12.—Preoperative catheterization studies in a case of patent ductus arteriosus. (Same reference as that for Fig. 10.)

Dr. Ferdinand McAllister: Walter McEfee is a 4-year-old boy who was brought into Vanderbilt Clinic for the first time at the age of 11 months, with a complaint of increasing cyanosis. There is nothing unusual about the past history or the mother's pregnancy. He was a full-term, normal child delivered by breech presentation. He was noted to be cyanotic at birth to a mild degree. This condition became increasingly apparent, and at the age of 8 months he began to have attacks of dyspnea and intense cyanosis, with lethargy. At the age of 11 months, he had an attack of tonsillitis, with a temperature of 103 F. It was necessary to hospitalize him at Lincoln Hospital at that time because of extreme cyanosis, and he was placed in an oxygen tent.

After this, he was referred to our clinic. On examination here, he was markedly cyanotic, demonstrated clubbing of the fingers and toes, and had a harsh systolic murmur to the left of the third interspace. The pulmonic second sound was said to be greater than the aortic second sound, and a roentgenogram of the heart showed a rather round shape with notching in the pulmonic area, some diminution in bronchovascular markings, and a shadow on the right in the supracardiac area (Fig. 14).

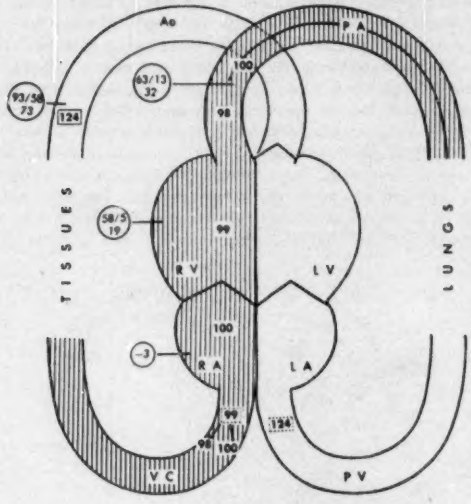


Fig. 13.—Postoperative catheterization studies in same case (five weeks). (Same reference as that for Fig. 10.)

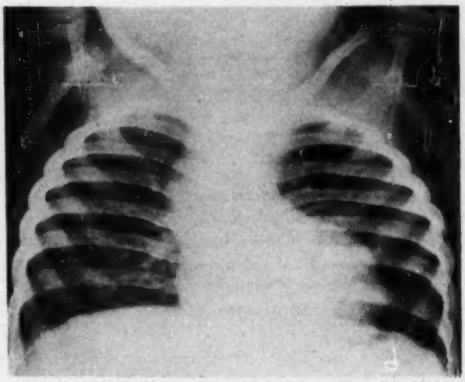


Fig. 14.—Roentgenogram of presented case of tetralogy of Fallot with right-sided aortic arch and interauricular septal defect.

The interpretation of the x-ray department was that the condition was congenital heart disease, type undetermined, with possible right-sided aortic arch. The electrocardiogram at the time showed left ventricular strain.

Because of the age of the child, it was decided that further investigative work or operation should not be done, and he was followed closely in Vanderbilt Clinic. During the next two and a half years, he showed progressive increase in cyanosis, with increasing disability. His hemoglobin level climbed to 21 gm. per 100 cc. Progressive polycythemia developed, and attacks of extreme cyanosis became more frequent. Finally, a year ago, he had two convulsive seizures, and because of this evidence of increased intercranial difficulty we decided to admit him at that time for catheterization.

This catheterization was done 10 months ago. On his admission, the hematocrit level was 87%, and it was necessary to perform phlebotomy twice, with plasma replacement, in order for catheter studies to be made. On catheterization, he demonstrated several of the factors which Dr. West has discussed. After the catheter was introduced into the right ventricle, it passed directly into the aorta, which was shown to lie on the right, and from there it went down to the level of the diaphragm. The blood in the aorta was 70% saturated. The catheter was then withdrawn into the right auricle and reintroduced, and this time it went into the left auricle and out into a pulmonary vein, demonstrating an interauricular septal defect. The blood was fully saturated. An incidental happening at catheterization was that the catheter also went into the coronary sinus, where the blood was 31% saturated.

These findings seemed to indicate that the patient had tetralogy of Fallot, with a right aortic arch, in addition to the interauricular septal defect. It was possible that he would be benefited by increasing the circulation to the lung, and he was operated on through an incision in the left side of the chest. The left pulmonary artery was seen to be under diminished pressure and contained a much reduced amount of blood.

The subclavian and carotid arteries on the left arose from a common trunk. The left subclavian artery was dissected as far as could be reached conveniently and divided, and the proximal stump was turned down and anastomosed end to side to the left pulmonary artery. The patient withstood the procedure fairly well, and the postoperative course was relatively uncomplicated. There was a considerable change in his skin color and in the color of the nail beds. Preoperatively his development, both physically and mentally, had been retarded. By the age of 2½, he was unable to walk except with support and could say no words. Since his operation he has gained 5 lb. (2.3 kg.), and he now plays with the other children to an increasing degree.

This case is presented, then, as an example of tetralogy of Fallot which illustrates that many of the cases are not straightforward and frequently have complicating factors such as those shown in this child, with interauricular septal defect and right-sided aorta. It also represents a case of successful treatment with the Blalock procedure.

DR. HUMPHREYS: The murmur that you hear now is the continuous murmur ordinarily associated with a ductus, in this case a surgical patent ductus.

DR. MCALLISTER: I do not know whether you can see his fingers, but the clubbing has diminished somewhat.

DR. HUMPHREYS: As you see, he is well nourished and looks like a normal child. Such patients show a startling recovery, but more recently another group has come to our attention in which, presumably, the result should be even better, since Walter still has his original lesion in his heart and in addition has what is at present a balanced or compensating lesion but a lesion which in itself carries some hazards and which may result ultimately in further trouble. The other lesion that I speak of is represented in Figure 6*A*, a pulmonary valvular stenosis with an auricular septal defect or rather a patent foramen ovale, so that back pressure allows some of the venous blood to escape through into the left side of the heart and enter the systemic circulation.

The child with this lesion was referred to us by a state agency in April, 1949. The parents had noted early in life that she panted excessively, but there was no cyanosis noted in early infancy. Cyanosis was first observed by her family physician when she was the age of 2½, and from that time onward it progressed. In other words, early in life there was relatively little shift through the foramen ovale; presumably the pressures here were not different from those in the other auricle. As time went on and she grew, the small orifice

at the pulmonary valve became relatively more of an obstruction and the pressure rose. Then more and more venous blood shifted over into the systemic circulation, as described by Dr. Richards. At 6 years of age she could hardly walk two blocks without squatting to rest. She was unable to keep up with her friends in ordinary activities at school, but she never had any serious cerebral symptoms such as the boy just shown. She never lost consciousness, nor had ever had any convulsions.

She was admitted to the hospital in February of this year, and at that time she showed mild clubbing and slight cyanosis, which became greater when she exercised. She squatted on the slightest excuse and for the most part preferred to sit around and not take part in any active play. There was a loud blowing systolic murmur in the pulmonary area, and the pulmonary second sound, the sound of valvular closure, could not be heard at all. The heart, as in the case of the first boy we showed, showed no abnormality in contour, but the pulmonary vascular markings were greatly diminished. She had a hemoglobin content of 17 gm. per 100 cc., a red blood cell count of 7,000,000 and a hematocrit value of 64%.

It was my impression that the patient might have a tetralogy, in which I was wrong, as was shown by the catheterization studies. The electrocardiogram showed a right ventricular hypertrophy, which was not of differential diagnostic assistance. When she was catheterized, however, the catheter passed readily into the right ventricle and a high reading was found. There was a systolic pressure of 201/16 in the right ventricle. The catheter was then passed into the pulmonary artery. It went into the right pulmonary artery, and then was withdrawn into the main pulmonary artery. What happened is notable. The inferior vena cava and right auricular oxygen saturations were 56, and since the catheter passed through the foramen ovale into the left auricle, as described by Dr. West, auricular blood then showed 70% saturation. However, when the catheter passed into the pulmonary artery, the first sample showed 36% oxygen and within a few minutes it was 23%, her color rapidly becoming extremely dark.

The catheter then had to be withdrawn into the right ventricle, because it was obvious that the orifice from the right ventricle into the pulmonary artery was scarcely larger than the catheter and the catheter was plugging it. On withdrawal of the catheter into the right ventricle, the saturation first went to 39, then to 55, and finally to 56, which was the level at the beginning. This result was, of course, a clear demonstration of her lesion, clearer than we often get or want.

The arterial saturation at that time was 77 when the catheter was not plugging the orifice, but during the period when the catheter plugged the orifice the peripheral arterial saturation fell below 50%, which indicates extreme cyanosis. The calculations showed that there was a 3-liter systemic blood flow and that exactly half of this passed through the interauricular septal defect and half through the pulmonary artery. In other words, the blood which entered the heart was divided in two; half of it went back out into the peripheral circulation and half of it through the pulmonary circulation.

The patient was subjected to pulmonary valvulotomy, devised by Dr. Brock two years ago, a theoretically simple operation in which the valve is cut and converted from a diaphragm or conical type of structure into a bivalve type. As might be expected, the result has been extremely satisfactory. This operation was performed about two months ago, and her heart still has a murmur. The valve, of course, is not normal, but it is no longer stenotic. You can see, I believe, that she has no cyanosis. The clubbing of her fingers is still apparent, although not marked. It probably will disappear completely within the next year. The murmur is a systolic one, without any sound of valvular closure over the pulmonary artery. It is somewhat softer than before operation, although it is surprising how little it changes in quality, considering the great changes in physiological balance that have been accomplished.

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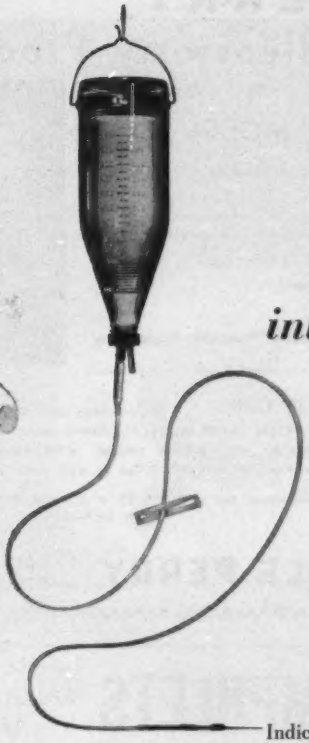

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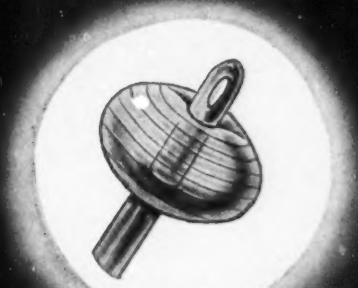

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